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CLINICAL PRACTICE GUIDELINES

2025 ACC/AHA/ACEP/NAEMSP/SCAI Guideline for the Management of Patients With Acute Coronary Syndromes: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

Developed in Collaboration With and Endorsed by the American College of Emergency Physicians, National Association of EMS Physicians, and Society for Cardiovascular Angiography and Interventions

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Aim: The "2025 ACC/AHA/ACEP/NAEMSP/SCAI Guideline for the Management of Patients With Acute Coronary Syndromes" incorporates new evidence since the "2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction" and the corresponding "2014 AHA/ACC Guideline for the Management of Patients With Non–ST-Elevation Acute Coronary Syndromes" and the "2015 ACC/AHA/SCAI Focused Update on Primary Percutaneous Coronary Intervention for Patients With ST-Elevation Myocardial Infarction." The "2025 ACC/AHA/ACEP/NAEMSP/SCAI Guideline for the Management of Patients With Acute Coronary Syndromes" and the "2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization" retire and replace, respectively, the "2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease."

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*Writing committee members are required to recuse themselves from voting on sections to which their specific relationships with industry may apply; see Appendix 1 for detailed information. †ACC/AHA Joint Committee on Clinical Practice Guidelines liaison. ‡Lay stakeholder/patient representative. §Society for Cardiovascular Angiography and Interventions representative. ‖American College of Emergency Physicians representative. ¶ACC/AHA joint staff representative. #National Association of EMS Physicians representative. **ACC/AHA Joint Committee on Performance Measures representative.

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Methods: A comprehensive literature search was conducted from July 2023 to April 2024. Clinical studies, systematic reviews and meta-analyses, and other evidence conducted on human participants were identified that were published in English from MEDLINE (through PubMed), EMBASE, the Cochrane Library, Agency for Healthcare Research and Quality, and other selected databases relevant to this guideline.

Structure: Many recommendations from previously published guidelines have been updated with new evidence, and new recommendations have been created when supported by published data.

Key Words: AHA Scientific Statements ■ acute coronary syndrome(s) ■ angina, unstable ■ anticoagulants ■ aspirin ■ atrial fibrillation ■ cardiovascular diseases ■ coronary artery disease ■ coronary syndrome ■ emergency medical services ■ EMS ■ fibrinolytic agents ■ hemorrhage ■ major adverse cardiovascular events ■ morphine ■ myocardial infarction ■ non–ST-segment elevation myocardial infarction ■ percutaneous coronary intervention ■ prehospital ■ revascularization ■ risk ■ ST-segment elevation myocardial infarction ■ time factors ■ treatment outcome

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TOP TAKE-HOME MESSAGES

1. Dual antiplatelet therapy is recommended for patients with acute coronary syndromes (ACS). Ticagrelor or prasugrel is recommended in preference to clopidogrel in patients with ACS who are undergoing percutaneous coronary intervention (PCI). In patients with non–ST-segment elevation ACS who are scheduled for an invasive strategy with timing of angiography to be >24 hours, upstream treatment with clopidogrel or ticagrelor may be considered to reduce major adverse cardiovascular events.
2. Dual antiplatelet therapy with aspirin and an oral P2Y12 inhibitor is indicated for at least 12 months as the default strategy in patients with ACS who are not at high bleeding risk. Several strategies are available to reduce bleeding risk in patients with ACS who have undergone PCI and require antiplatelet therapy: (a) in patients at risk for gastrointestinal bleeding, a proton pump inhibitor is recommended; (b) in patients who have tolerated dual antiplatelet therapy with ticagrelor, transition to ticagrelor monotherapy is recommended ≥1 month after PCI; or (c) in patients who require long-term anticoagulation, aspirin discontinuation is recommended 1 to 4 weeks after PCI with continued use of a P2Y12 inhibitor (preferably clopidogrel).
3. High-intensity statin therapy is recommended for all patients with ACS, and with the option to initiate concurrent ezetimibe. A nonstatin lipid-lowering agent (eg, ezetimibe, evolocumab, alirocumab, inclisiran, bempedoic acid) is recommended for patients already on maximally tolerated statin who have a low-density lipoprotein cholesterol level of ≥70 mg/dL (1.8 mmol/L). It is reasonable in this high-risk population to further intensify lipid-lowering therapy if the low-density lipoprotein cholesterol level is 55 to <70 mg/dL (1.4 to <1.8 mmol/L) and patient is already on a maximally tolerated statin.
4. In patients with non–ST-segment elevation ACS who are at intermediate or high risk of ischemic events, an invasive approach with the intent to proceed with revascularization is recommended during hospitalization to reduce major adverse cardiovascular events. In patients with non–ST-segment elevation ACS who are at low risk of ischemic events, a routine invasive or selective invasive approach with further risk stratification is recommended to help identify those who may require revascularization and to reduce major adverse cardiovascular events.
5. Two procedural strategies are recommended in patients with ACS who are undergoing PCI: (a) radial approach is preferred over femoral approach in patients with ACS undergoing PCI to reduce bleeding, vascular complications, and death; and (b) intracoronary imaging is recommended to guide PCI in patients with ACS with complex coronary lesions.

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6. A strategy of complete revascularization is recommended in patients with ST-segment elevation myocardial infarction or non–ST-segment elevation ACS. The choice of revascularization method (ie, coronary artery bypass graft surgery versus multivessel PCI) in non–ST-segment elevation ACS and multivessel disease should be based on the complexity of the coronary artery disease and comorbid conditions. PCI of significant nonculprit stenoses for patients with ST-segment elevation myocardial infarction can be performed in a single procedure or staged with some preference toward performing multivessel PCI in a single procedure. In patients with ACS and cardiogenic shock, emergency revascularization of the culprit vessel is indicated; however, routine PCI of non–infarct-related arteries at the time of PCI is not recommended.
7. Based on one trial, use of the microaxial flow pump in selected patients with cardiogenic shock related to acute myocardial infarction is reasonable to reduce death. However, complications such as bleeding, limb ischemia, and renal failure are higher with the microaxial flow pump compared with usual care. Therefore, careful attention to vascular access and weaning of support is important to appropriately balance the benefits and risks.
8. Red blood cell transfusion to maintain a hemoglobin of 10 g/dL may be reasonable in patients with ACS and acute or chronic anemia who are not actively bleeding.
9. After discharge, focus on secondary prevention is fundamental. A fasting lipid panel is recommended 4 to 8 weeks after initiating or adjusting the dose of lipid-lowering therapy. Referral to cardiac rehabilitation is also recommended, with the option for home-based programs for patients unable or unwilling to attend in person.

PREAMBLE

Since 1980, the American College of Cardiology (ACC) and American Heart Association (AHA) have translated scientific evidence into clinical practice guidelines with recommendations to improve cardiovascular health. These guidelines, which are based on systematic methods to evaluate and classify evidence, provide a foundation for the delivery of quality cardiovascular care. The ACC and AHA sponsor the development and publication of clinical practice guidelines without commercial support, and members volunteer their time to the writing and review efforts. Guidelines are official policy of the ACC and AHA. For some guidelines, the ACC and AHA collaborate with other organizations.

Intended Use

Clinical practice guidelines provide recommendations applicable to patients with or at risk of developing cardiovascular disease (CVD). The focus is on medical practice in the United States, but these guidelines are relevant to patients throughout the world. Although guidelines may be used to inform regulatory or payer decisions, the intent is to improve quality of care and align with patients' interests. Guidelines are intended to define practices meeting the needs of patients in most, but not all, circumstances and should not replace clinical judgment.

Clinical Implementation

Management, in accordance with guideline recommendations, is effective only when followed by both practitioners and patients. Adherence to recommendations can be enhanced by shared decision-making between clinicians and patients, with patient engagement in selecting interventions on the basis of individual values, preferences, and associated conditions and comorbidities.

Methodology and Modernization

The ACC/AHA Joint Committee on Clinical Practice Guidelines (Joint Committee) continuously reviews, updates, and modifies guideline methodology on the basis of published standards from organizations, including the National Academy of Medicine (formerly the Institute of Medicine),[1] and on the basis of internal reevaluation. Similarly, presentation and delivery of guidelines are reevaluated and modified in response to evolving technologies and other factors to optimally facilitate dissemination of information to health care professionals at the point of care.

Numerous modifications to the guidelines have been implemented to make them shorter and enhance "user friendliness." Guidelines are written and presented in a modular, "knowledge chunk" format in which each chunk includes a table of recommendations, a brief synopsis, recommendation-specific supportive text, and, when appropriate, flow diagrams or additional tables. Hyperlinked references are provided for each modular knowledge chunk to facilitate quick access and review.

In recognition of the importance of cost–value considerations, in certain guidelines, when appropriate and feasible, an assessment of value for a drug, device, or intervention may be performed in accordance with the ACC/AHA methodology.[2]

To ensure that guideline recommendations remain current, new data will be reviewed on an ongoing basis by the writing committee and staff. When applicable,

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recommendations will be updated with new evidence, or new recommendations will be created when supported by published evidence-based data. Going forward, targeted sections/knowledge chunks will be revised dynamically after publication and timely peer review of potentially practice-changing science. The previous designations of "full revision" and "focused update" have been phased out. For additional information and policies on guideline development, readers may consult the ACC/AHA guideline methodology manual[3] and other methodology articles.[4–6]

Selection of Writing Committee Members

The Joint Committee strives to ensure that the guideline writing committee contains requisite content expertise and is representative of the broader cardiovascular community by selection of experts across a spectrum of backgrounds, representing different geographic regions, sexes, races, ethnicities, intellectual perspectives/biases, and clinical practice settings. Organizations and professional societies with related interests and expertise are invited to participate as collaborators.

Relationships With Industry and Other Entities

The ACC and AHA have rigorous policies and methods to ensure that documents are developed without bias or improper influence. The complete policy on relationships with industry and other entities (RWI) can be found at https://www.acc.org/guidelines/about-guidelines-and-clinical-documents/relationships-with-industry-policy. Appendix 1 of the guideline lists writing committee members' comprehensive and relevant RWI; for the purposes of full transparency, comprehensive and relevant disclosure information for the Joint Committee is also available at https://www.acc.org/guidelines/about-guidelines-and-clinical-documents/guidelines-and-documents-task-forces.

Evidence Review and Evidence Review Committees

In developing recommendations, the writing committee uses evidence-based methodologies that are based on all available data.[3,4] Literature searches focus on randomized controlled trials (RCTs) but also include registries, nonrandomized comparative and descriptive studies, case series, cohort studies, systematic reviews, and expert opinion. Only key references are cited.

An independent evidence review committee is commissioned when there are ≥1 questions deemed of utmost clinical importance and merit formal systematic review to determine which patients are most likely to benefit from a drug, device, or treatment strategy, and to what degree. Criteria for commissioning an evidence review committee and formal systematic review include absence of a current authoritative systematic review, feasibility of defining the benefit and risk in a time frame consistent with the writing of a guideline, relevance to a substantial number of patients, and likelihood that the findings can be translated into actionable recommendations. Evidence review committee members may include methodologists, epidemiologists, clinicians, and biostatisticians. Recommendations developed by the writing committee on the basis of the systematic review are marked "SR."

Guideline-Directed Medical Therapy

The term guideline-directed medical therapy encompasses clinical evaluation, diagnostic testing, and both pharmacological and procedural treatments. For these and all recommended drug treatment regimens, the reader should confirm dosage with product insert material and evaluate for contraindications and interactions. Recommendations are limited to drugs, devices, and treatments approved for clinical use in the United States.

Catherine M. Otto, MD, FACC, FAHA
Chair, ACC/AHA Joint Committee on
Clinical Practice Guidelines

1. INTRODUCTION

1.1. Methodology and Evidence Review

The recommendations listed in this guideline are, whenever possible, evidence based. An initial extensive evidence review—which included literature derived from research involving human subjects, published in English, and indexed in MEDLINE (through PubMed), EMBASE, the Cochrane Library, the Agency for Healthcare Research and Quality, and other selected databases relevant to this guideline—was conducted from July 2023 to April 2024. Key search words included but were not limited to the following: AHA/ACC Clinical Practice Guidelines; acute coronary syndrome(s); angina, unstable; anticoagulants; aspirin; atrial fibrillation; cardiovascular diseases; coronary artery disease (CAD); coronary syndrome; emergency medical services; fibrinolytic agents; hemorrhage; major adverse cardiovascular events (MACE); morphine; myocardial infarction; non–ST-elevation myocardial infarction (NSTEMI); percutaneous coronary intervention (PCI); prehospital; revascularization; risk; ST-elevation myocardial infarction (STEMI); time factors; treatment outcome.

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Additional relevant studies, which were published through April 2024 during the guideline writing process, were also considered by the writing committee and added to the evidence tables when appropriate. The final evidence tables summarize the evidence used by the writing committee to formulate recommendations. References selected and published in the present document are representative and not all-inclusive.

1.2. Composition of the Writing Committee

The writing committee consisted of general cardiologists, interventional cardiologists, cardiovascular surgeons, critical care cardiologists, emergency physicians, cardiac imaging experts, advanced practice nurses, clinical pharmacists, and lay/patient representatives. The writing committee included representatives from the AHA, ACC, American College of Emergency Physicians (ACEP), National Association of EMS Physicians (NAEMSP), and Society for Cardiovascular Angiography and Interventions (SCAI). Appendix 1 of the current document lists writing committee members' comprehensive and relevant RWI.

1.3. Guideline Review and Approval

The Joint Committee appointed a peer review committee to review the document. The peer review committee comprised individuals nominated by the ACC, AHA, and the collaborating organizations. Reviewers' RWI information was distributed to the writing committee and is published in this document (Appendix 2). This document was approved for publication by the governing bodies of the ACC and the AHA and was endorsed by ACEP, NAEMSP, and SCAI.

1.4. Scope of the Guideline

The scope of the "2025 ACC/AHA/ACEP/NAEMSP/SCAI Guideline for the Management of Patients With Acute Coronary Syndromes" (referred to hereafter as the "2025 ACS guideline") is to incorporate new evidence since the publication of the "2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction,"[1] the corresponding "2014 AHA/ACC Guideline for the Management of Patients With Non–ST-Elevation Acute Coronary Syndromes,"[2] and the "2015 ACC/AHA/SCAI Focused Update on Primary Percutaneous Coronary Intervention for Patients With ST-Elevation Myocardial Infarction."[3] The 2025 ACS guideline and the "2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization"[4] retire and replace, respectively, the "2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease."[5] This guideline primarily focuses on the management of type 1 acute myocardial infarction (AMI). It can be challenging to differentiate type 1 versus type 2 MI. In cases of uncertainty and depending on the benefits/risks of a specific diagnostic or therapeutic intervention, it may be appropriate to err on the side of considering an event a type 1 acute coronary syndrome (ACS) event until established to be otherwise.

In the United States, an estimated 805 000 AMIs occur annually of which 605 000 are first MI events and 200 000 are recurrent.[6–8] Although significant morbidity and mortality are associated with MI, 30-day and in-hospital mortality rates after ST-segment elevation myocardial infarction (STEMI) have declined in part as a result of timely reperfusion and implementation of evidence-based secondary prevention.[9] From 2011 to 2021 in the United States, the annual death rate attributable to coronary heart disease declined by 15.0%.[6] The economic impact of MI is also substantial, with the total annual cost estimated at $84.9 billion, including direct medical expenditures and indirect lost productivity and wages.[10,11] The incidence of MI is higher among Black males compared with non-Hispanic White males for reasons that are believed to be multifactorial.[12,13] Potential factors that may contribute to this disparity include a higher prevalence of risk factors for CAD, less use of guideline-recommended medications post-MI, and socioeconomic factors.[14–19] In addition to racial disparities, there are sex-related disparities in the prevalence, presentation, treatment, and outcomes of ACS even after adjusting for confounding factors such as income, geography, and education.[20] Women tend to present with ACS on average 10 years later than men and with a greater burden of CVD risk factors. Although chest pain remains the most common symptom of AMI, women are more likely than men to present with accompanying non–chest pain symptoms.[21–24] A delay in recognition of these symptoms can result in delays in presentation, diagnosis, and timely treatment of women with ACS. Studies have also shown that women presenting with ACS are less likely to be correctly diagnosed with an ACS, receive guideline-directed medical therapy,[25–27] and/or undergo coronary revascularization when indicated.[28,29] Bridging these racial and sex gaps will require continued provider education, better understanding of barriers to accessing quality care and guideline-directed medical therapy, and changes at the community and legislative level to address social determinants of health such as income, employment status, neighborhood safety, and access to healthy foods.

In developing the 2025 ACS guideline, the writing committee reviewed previously published guidelines and related scientific statements. Table 1 contains a list of these publications deemed pertinent to this writing effort. It is intended for use as a resource, obviating

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Table 1. Associated Publications

Title	Organization	Publication Year (Reference)
Guidelines		
Management of blood cholesterol	AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA	2018[30]
Prevention, detection, evaluation, and management of high blood pressure in adults	ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA	2018[31]
Primary prevention of cardiovascular disease	ACC/AHA	2019[32]
Coronary artery revascularization	ACC/AHA/SCAI	2021[4]
Evaluation and diagnosis of chest pain	AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR	2021[33]
Prevention of stroke in patients with stroke and transient ischemic attack	AHA/ASA	2021[34]
Management of heart failure	AHA/ACC/HFSA	2022[35]
Management of patients with chronic coronary disease	AHA/ACC/ACCP/ASPC/NLA/PCNA	2023[36]
Diagnosis and management of atrial fibrillation	ACC/AHA/ACCP/HRS	2023[37]
Other Relevant Documents		
Home-based cardiac rehabilitation	AHA/ACC/AACVPR	2019[38]
Classification of cardiogenic shock	SCAI, endorsed by ACC/AHA/SCCM/STS	2019[39]
Contemporary diagnosis and management of patients with myocardial infarction in the absence of obstructive coronary artery disease	AHA	2019[40]
Invasive management of acute myocardial infarction complicated by cardiogenic shock	AHA	2021[41]
Mechanical complications of acute myocardial infarction	AHA	2021[42]
SHOCK stage classification update	SCAI, endorsed by ACC/ACEP/AHA/ESC/ACVC/ISHLT/ SCCM/STS	2021[43]
Management of patients at risk for and with left ventricular thrombus	AHA	2022[44]
Cardiac catheterization laboratory management of the comatose adult patient with an out-of-hospital cardiac arrest	AHA	2024[45]

AACVPR indicates American Association of Cardiovascular and Pulmonary Rehabilitation; AAPA, American Academy of Physician Associates (formerly American Academy of Physician Assistants); ABC, Association of Black Cardiologists; ACC, American College of Cardiology; ACCP, American College of Clinical Pharmacy; ACEP, American College of Emergency Physicians; ACPM, American College of Preventive Medicine; ACVC, Association for Acute Cardiovascular Care; ADA, American Diabetes Association; AGS, American Geriatrics Society; AHA, American Heart Association; APhA, American Pharmacists Association; ASA, American Stroke Association; ASCVD, atherosclerotic cardiovascular disease; ASE, American Society of Echocardiography; ASH, American Society of Hypertension; ASPC, American Society for Preventive Cardiology; CHEST, American College of Chest Physicians; ESC, European Society of Cardiology; HFSA, Heart Failure Society of America; HRS, Heart Rhythm Society; ISHLT, International Society for Heart and Lung Transplantation; NLA, National Lipid Association; NMA, National Medical Association; PCNA, Preventive Cardiovascular Nurses Association; SAEM, Society for Academic Emergency Medicine; SCAI, Society for Cardiovascular Angiography and Interventions; SCCM, Society of Critical Care Medicine; SCCT, Society of Cardiovascular Computed Tomography; SCMR, Society for Cardiovascular Magnetic Resonance; SHOCK, Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock trial; and STS, Society of Thoracic Surgery.

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the need to repeat existing guideline recommendations. Some recommendations have been carried forward from previously published guidelines. If unchanged, those recommendations remain current. Any changes to the formatting or content of these recommendations are defined as:

- Modified: formatting changes (eg, minor verbiage modifications such as PICO[TS] structure)
- Adapted: substantive changes (eg, major adaptations, such as a change in Class of Recommendation [COR], Level of Evidence [LOE], drug, or device classification).

Changes are depicted in a footnote below the recommendation tables.

1.5. Class of Recommendation and Level of Evidence

The COR indicates the strength of recommendation, encompassing the estimated magnitude and certainty of benefit in proportion to risk. The LOE rates the quality of scientific evidence supporting the intervention on the basis of the type, quantity, and consistency of data from clinical trials and other sources (Table 2).[1]

Table 2. Applying the American College of Cardiology/American Heart Association Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care* (Updated May 2019)

CLASS (STRENGTH) OF RECOMMENDATION	
CLASS 1 (STRONG)	**Benefit >>> Risk**
Suggested phrases for writing recommendations: • Is recommended • Is indicated/useful/effective/beneficial • Should be performed/administered/other • Comparative-Effectiveness Phrases†: – Treatment/strategy A is recommended/indicated in preference to treatment B – Treatment A should be chosen over treatment B	
CLASS 2a (MODERATE)	**Benefit >> Risk**
Suggested phrases for writing recommendations: • Is reasonable • Can be useful/effective/beneficial • Comparative-Effectiveness Phrases†: – Treatment/strategy A is probably recommended/indicated in preference to treatment B – It is reasonable to choose treatment A over treatment B	
CLASS 2b (WEAK)	**Benefit ≥ Risk**
Suggested phrases for writing recommendations: • May/might be reasonable • May/might be considered • Usefulness/effectiveness is unknown/unclear/uncertain or not well-established	
CLASS 3: No Benefit (MODERATE) **(Generally, LOE A or B use only)**	**Benefit = Risk**
Suggested phrases for writing recommendations: • Is not recommended • Is not indicated/useful/effective/beneficial • Should not be performed/administered/other	
Class 3: Harm (STRONG)	**Risk > Benefit**
Suggested phrases for writing recommendations: • Potentially harmful • Causes harm • Associated with excess morbidity/mortality • Should not be performed/administered/other	

LEVEL (QUALITY) OF EVIDENCE‡	
LEVEL A	
• High-quality evidence‡ from more than 1 RCT • Meta-analyses of high-quality RCTs • One or more RCTs corroborated by high-quality registry studies	
LEVEL B-R	**(Randomized)**
• Moderate-quality evidence‡ from 1 or more RCTs • Meta-analyses of moderate-quality RCTs	
LEVEL B-NR	**(Nonrandomized)**
• Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies • Meta-analyses of such studies	
LEVEL C-LD	**(Limited Data)**
• Randomized or nonrandomized observational or registry studies with limitations of design or execution • Meta-analyses of such studies • Physiological or mechanistic studies in human subjects	
LEVEL C-EO	**(Expert Opinion)**
• Consensus of expert opinion based on clinical experience	

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR 1 and 2a; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely-used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

1.6. Abbreviations

Abbreviation	Meaning/Phrase
ACEi	angiotensin-converting enzyme inhibitor
ACS	acute coronary syndromes
AF	atrial fibrillation
AMI	acute myocardial infarction
ARB	angiotensin receptor blocker
ASCVD	atherosclerotic cardiovascular disease
CABG	coronary artery bypass grafting
CAD	coronary artery disease
CCD	chronic coronary disease
CDP	clinical decision pathway
CICU	cardiac intensive care unit
CR	cardiac rehabilitation
cTn	cardiac troponin
CVD	cardiovascular disease
DAPT	dual antiplatelet therapy
DOAC	direct oral anticoagulant
ECG	electrocardiogram
FDA	US Food and Drug Administration
FFR	fractional flow reserve

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Circulation. 2025;151:e00–e00. DOI: 10.1161/CIR.0000000000001309

Abbreviation	Meaning/Phrase
FMC	first medical contact
GLP-1	glucagon-like peptide-1
HF	heart failure
hs-cTn	high-sensitivity cardiac troponin
IABP	intra-aortic balloon pump
ICD	implantable cardioverter-defibrillator
IVUS	intravascular ultrasound
LDL	low-density lipoprotein
LDL-C	low-density lipoprotein cholesterol
LV	left ventricular
LVEF	left ventricular ejection fraction
MACE	major adverse cardiovascular event
MCS	mechanical circulatory support
MI	myocardial infarction
MINOCA	MI with nonobstructive coronary artery disease
MVD	multivessel disease
NSTE-ACS	non–ST-segment elevation ACS
NSTEMI	non–ST-segment elevation myocardial infarction
OCT	optical coherence tomography
OR	odds ratio
PCI	percutaneous coronary intervention
PCSK9	proprotein convertase subtilisin/kexin type 9
PPCI	primary percutaneous coronary intervention
PPI	proton pump inhibitor
QOL	quality of life
RCT	randomized controlled trial
ROSC	return of spontaneous circulation
SGLT-2	sodium-glucose cotransporter-2
STEMI	ST-segment elevation myocardial infarction
UFH	unfractionated heparin
VA-ECMO	venoarterial extracorporeal membrane oxygenation

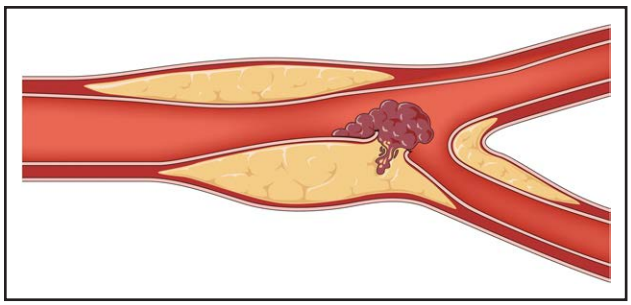

Figure 1. Pathobiology of a Type 1 Myocardial Infarction Due to Atherosclerotic Plaque Disruption.
Progressive lipid accumulation and inflammation within an atherosclerotic plaque may lead to plaque instability. Rupture or erosion of the atherosclerotic plaque and exposure of plaque contents to the circulation may then culminate in activation of the coagulation cascade and subsequent thrombosis. When this occurs in the epicardial vessels of the coronary circulation, the presence of thrombus may compromise flow to the myocardium, leading to myocardial ischemia and eventual myonecrosis. Illustration by Patrick Lane, ScEYEnce Studios. Copyright 2025 American College of Cardiology Foundation, and American Heart Association, Inc.

2. OVERVIEW OF ACS

2.1. Definition and Classification of ACS

ACS are typically caused by the disruption (rupture or erosion) of an unstable coronary artery atherosclerotic plaque with associated partial or complete coronary artery thrombosis and/or microemboli, resulting in diminished blood flow to the myocardium and subsequent myocardial ischemia (Figure 1).[1,2] ACS includes 3 related clinical conditions that exist along a continuum of severity: (1) unstable angina, (2) non–ST-segment elevation myocardial infarction (NSTEMI), and (3) STEMI. The initial diagnosis and classification of ACS should be based on the clinical history and symptomatology, interpretation of the ECG (Table 3), and assessment of cardiac troponin (cTn). Unstable angina is defined by transient myocardial ischemia leading to diminished flow in the absence of significant myonecrosis detected by circulating troponin. In contrast, patients with more prolonged or severe myocardial ischemia are diagnosed with MI and have elevated biomarkers of myonecrosis. Patients with NSTEMI may have a partially occluded coronary artery leading to subendocardial ischemia, while those with STEMI typically have a completely occluded vessel leading to transmural myocardial ischemia and infarction (Figure 2).[3,4] The pathophysiology of ACS can be dynamic and thus patients can rapidly progress from one clinical condition (eg, unstable angina, NSTEMI, STEMI) to another during the course of their presentation and initial evaluation and treatment. Other, less common causes of myocardial ischemia, among others, include coronary artery spasm, embolism, and dissection.[3]

This guideline will focus on the acute management of ACS, including unstable angina, NSTEMI, and STEMI, which are presumed to result from atherosclerotic plaque rupture or plaque erosion and subsequent thrombosis.[4] Under the Universal Definition of MI, these MI events would be classified as type 1 MI events (Table 4).[4] The diagnostic evaluation of chest pain and the management of type 2 MI, spontaneous coronary artery dissection, and MINOCA (MI with nonobstructive coronary artery disease) are covered in separate documents.[5–8] A detailed description of the approach to the evaluation of patients with chest pain can be found in the 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Chest Pain Guideline.[5]

Progressive lipid accumulation and inflammation within an atherosclerotic plaque may lead to plaque instability.[1] Rupture of the atherosclerotic plaque and exposure of plaque contents to the circulation may then culminate in activation of the coagulation cascade and subsequent thrombosis. The presence of thrombus may compromise flow to the myocardium, leading to myocardial ischemia and eventual myonecrosis. Since early initiation of therapy is imperative for patients with ACS, a

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Table 3. Electrocardiographic Interpretation for Patients With Suspected Acute Coronary Syndromes

	NSTE-ACS	STEMI
Electrocardiographic evidence of ischemia	New or presumed new and usually dynamic horizontal or downsloping ST-segment depression ≥0.5 mm in ≥2 contiguous leads and/or T-wave inversion >1 mm in ≥2 contiguous leads with prominent R wave or R/S ratio >1 or transient ST-segment elevation.	New or presumed new ST-elevation of ≥1 mm in ≥2 anatomically contiguous leads (measured at the J-point) in all leads other than V2-V3 and ≥2 mm in men ≥40 y, ≥2.5 mm in men <40 y, and ≥1.5 mm in women regardless of age in leads V2-V3.*
Other observed electrocardiographic changes	Many patients with NSTE-ACS have either nonspecific ST-segment or T-wave changes or a normal ECG. The absence of electrocardiographic evidence of ischemia does not exclude ACS.	Posterior leads (V7-V9) should be obtained in patients with suspected left circumflex occlusion particularly in the setting of isolated ST-segment depression ≥0.5 mm in leads V1-V3.

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*ST-segment changes may be observed in other conditions including acute pericarditis, left ventricular hypertrophy, LBBB, Brugada syndrome, right ventricular pacing, Takotsubo syndrome, and early repolarization that may obscure the diagnosis of STEMI.[12] New or presumably new LBBB at presentation occurs infrequently and should not be considered diagnostic of AMI in isolation; clinical correlation is required.[13] A new LBBB in an asymptomatic patient does not constitute a STEMI equivalent.[11]

ACS indicates acute coronary syndromes; AMI, acute myocardial infarction, LBBB, left bundle branch block; NSTE-ACS, non–ST-segment elevation ACS; and STEMI, ST-segment elevation MI.

high index of suspicion is warranted for those who present with signs and symptoms that could be consistent with myocardial ischemia.

Patients with ACS are at the highest risk for cardiovascular complications acutely, including prior to hospital presentation and during the early hospital phase. With appropriate management, this risk begins to attenuate; however, patients remain at increased risk of recurrent cardiovascular events for several months to years after an ACS.[9] This may in part be related to the acute inflammatory milieu that exists after ACS that may contribute to a heightened risk of recurrent events. Although the point at which a patient transitions from being a patient with an acute ACS to one with more stable or chronic coronary disease (CCD) is incompletely defined, many of the medications indicated at discharge in patients with an ACS are similar to those for the management of a patient with CCD and should be extended more than a year beyond ACS. The long-term management of patients with ACS who are presumed to now have more stable coronary disease has been described in the 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Chronic Coronary Disease Guideline.[10]

3. INITIAL EVALUATION AND MANAGEMENT OF SUSPECTED ACS

3.1. Initial Assessment of Suspected ACS

3.1.1. Prehospital Assessment and Management Considerations for Suspected ACS

Recommendations for Prehospital Assessment and Management Considerations for Suspected ACS
Referenced studies that support recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
Suspected ACS		
1	B-NR	1. In patients with suspected ACS, a 12-lead ECG should be acquired and interpreted within 10 minutes of first medical contact (FMC)* to identify patients with STEMI.[1,2]
1	C-LD	2. In patients with suspected ACS in which the initial ECG is nondiagnostic of STEMI, serial ECGs to detect potential ischemic changes should be performed, especially when clinical suspicion of ACS is high, symptoms are persistent, or the clinical condition deteriorates.†[3,4]
STEMI		
1	B-NR	3. In patients with suspected STEMI, immediate emergency medical services (EMS) transport to a PCI-capable hospital for primary PCI (PPCI‡) is the recommended triage strategy, with an FMC–to-first-device time system goal of ≤90 minutes.[5–7]
1	B-NR	4. In patients with suspected STEMI, early advance notification of the receiving PCI-capable hospital by EMS personnel and activation of the cardiac catheterization team is recommended to reduce time to reperfusion.[1,8,9]

*FMC indicates the time point when the patient is initially assessed by a health care professional who can obtain and interpret the ECG and deliver initial interventions (eg, defibrillation).

†Modified from the "2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain."[10]

‡PPCI refers to emergency PCI in the setting of STEMI to achieve reperfusion in patients without previous fibrinolytic treatment.

Synopsis

Rapid and coordinated prehospital care plays a critical role in the optimal management of patients with suspected ACS.[11] Patients with suspected ACS should be transported to the emergency department (ED) by emergency medical services (EMS).[12] In contrast to transport by private vehicle, EMS transport allows for assessment, monitoring, and treatment of potentially life-threatening conditions such as arrhythmias or cardiac arrest during transport to the ED.[13] In patients with suspected ACS, trained prehospital personnel should obtain a focused history and physical examination (including assessment of vital signs) and obtain at least one 12-lead ECG so that the electrocardiographic findings can facilitate next steps in

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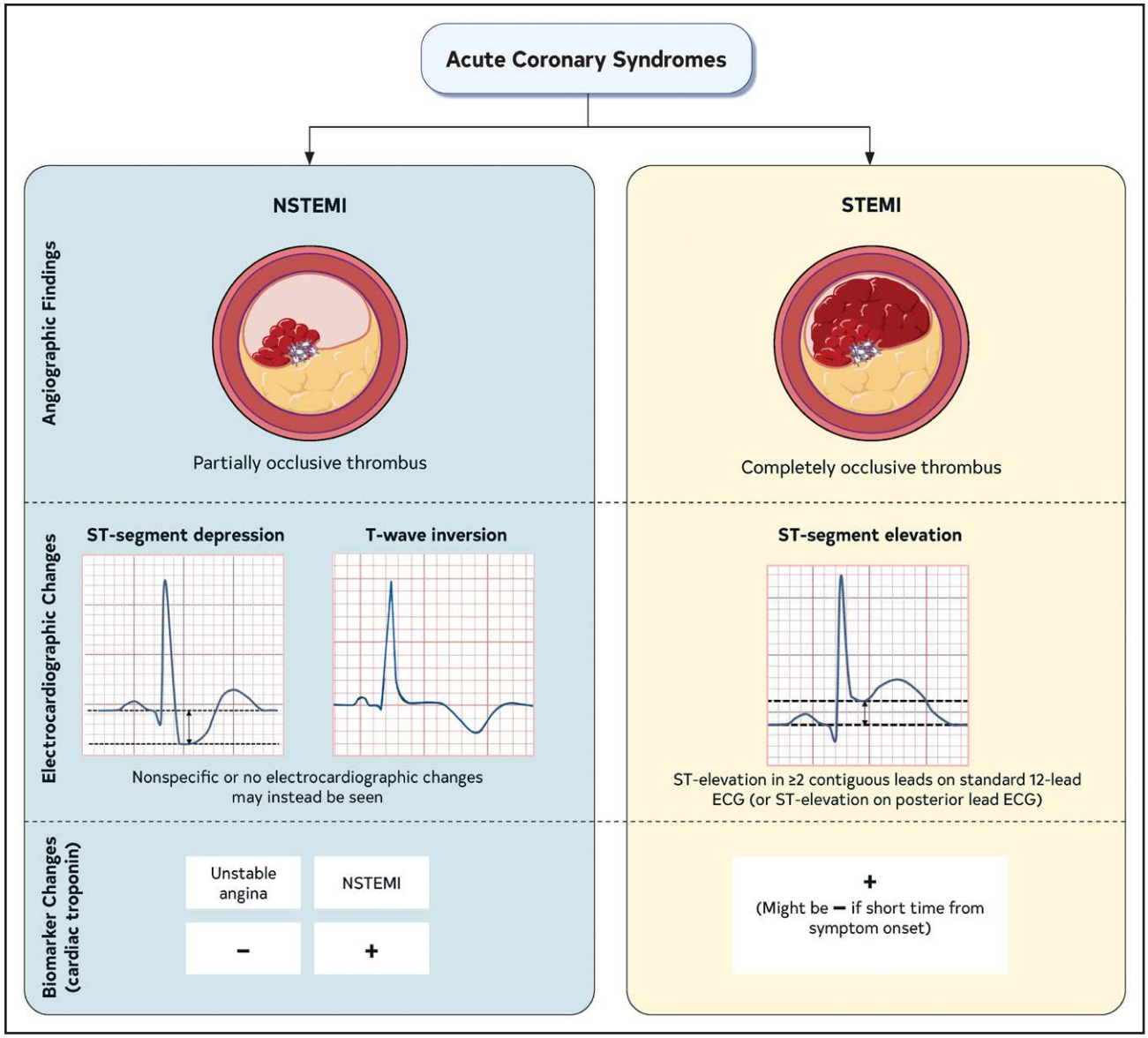

Figure 2. Types and Classification of Acute Coronary Syndromes.
NSTEMI indicates non–ST-segment elevation myocardial infarction; and STEMI, ST-segment elevation myocardial infarction.
Illustration by Patrick Lane, ScEYEnce Studios. Copyright 2025 American College of Cardiology Foundation, and the American Heart Association, Inc.

patient triage. Specifically, patients should be managed based on the presence or absence of ST-segment elevation (or suspected equivalent) on the 12-lead ECG (Table 3 for STEMI electrocardiographic criteria). When possible, electrocardiographic tracings can be transmitted to the PPCI center while en route to help expedite coronary reperfusion upon arrival. Because patients with ACS and evidence of heart failure (HF), ventricular arrhythmias, or cardiogenic shock in the prehospital setting are at highest risk for death, identification of these complications is important with subsequent triage of these patients to a PCI-capable facility when possible (Section 8, "Cardiogenic Shock Management").[14,15]

Recommendation-Specific Supportive Text

1. The early acquisition and recording of prehospital 12-lead ECGs by trained personnel is associated with shorter reperfusion times and lower mortality rates from STEMI if this diagnostic information is integrated in patients' care.[1,2,16] Appropriately trained EMS personnel (ie, paramedics) can interpret 12-lead ECGs for the identification of STEMI

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Table 4. Types of Acute Myocardial Infarction According to the Universal Definition of Myocardial Infarction

Type 1*	**Caused by acute coronary atherothrombosis, usually precipitated by atherosclerotic plaque disruption (rupture or erosion) and often associated with partial or complete vessel thrombosis.**
Type 2	Caused by an imbalance between myocardial oxygen supply and demand unrelated to acute coronary atherothrombosis.
Type 3	Cardiac death, with symptoms of myocardial ischemia and presumed ischemic electrocardiographic changes or ventricular arrythmia, before blood samples for cardiac biomarkers can be obtained or increases in cardiac biomarkers can be identified and/or in whom MI is identified by autopsy.
Type 4	4a: Peri-PCI MI caused by a procedural complication and detected ≤48 h after PCI. 4b: Post-PCI MI caused by coronary stent or stent scaffold thrombosis. 4c: Post-PCI MI caused by coronary stent restenosis.
Type 5	Peri-CABG MI caused by a procedural complication detected ≤48 h after CABG surgery.

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*This guideline focuses on the management of type 1 AMI. The diagnostic evaluation of chest pain and the management of type 2 MI, SCAD, and MINOCA are covered in separate documents.[5–8]

AMI indicates acute myocardial infarction; CABG, coronary artery bypass grafting; MI, myocardial infarction; MINOCA, MI with nonobstructive coronary artery disease; PCI, percutaneous coronary intervention; and SCAD, spontaneous coronary artery dissection.

with high accuracy.[17] When ST-segment elevation or an equivalent finding is present on the initial ECG (Table 3), initial management and triage should follow the prescribed STEMI treatment algorithm. Electrocardiographic changes are not required to confirm a diagnosis of non–ST-segment elevation ACS (NSTE-ACS).

2. In patients for whom the initial ECG is nondiagnostic, serial ECGs should be performed during transport to the hospital especially when clinical suspicion of ACS is high, ischemic symptoms are persistent, or the clinical condition deteriorates.[3,4] Acquisition of subsequent ECGs should not delay transport to a hospital. A second and/or third ECG during EMS transport may identify up to 15% of additional STEMI cases not present on the first ECG.[3] In an observational study of 728 patients with suspected ACS who underwent serial prehospital ECGs, a STEMI diagnosis was subsequently made in 8% of patients following an initial nondiagnostic ECG with a median of 12 minutes after the first study.[4] Posterior ECG leads (V7-V9) should be applied in patients with ongoing symptoms and a nondiagnostic ECG and those with ST-segment depressions in leads V1-V3 to assess for ST-segment elevation in the posterior leads, which could indicate a posterior STEMI.
3. PPCI is the preferred method of reperfusion for patients with STEMI.[18] Rapid reperfusion of the infarct-related artery is associated with improved myocardial salvage and improved survival.[19,20] For those who are managed by PPCI, each 30 minutes of delay is associated with an increase in the relative risk of 1-year mortality by 7.5%.[19] As such, evidence supports system-level interventions to reduce time-to-device.[11] Patients with prehospital identification of STEMI should preferentially be transported to a PCI-capable hospital with a goal of FMC–to–first-device time of ≤90 minutes.[20] For patients who are directly transported to the hospital by EMS, the time to treatment goal is defined as the FMC by EMS until coronary reperfusion. Direct transfer to a PCI-capable facility has been associated with shorter reperfusion times and lower mortality compared with transport to the closest non–PCI-capable hospital.[21] In prehospital settings where a FMC–to–first-device goal of ≤90 minutes is not feasible in patients with STEMI, direct transport to a PCI-capable hospital may be considered if the anticipated FMC-to-device time is ≤120 minutes.[22,23] See Section 5.1, "Regional Systems of STEMI Care," for further details.
4. The implementation of several care processes has demonstrated significant reductions in reperfusion times in patients with STEMI when implemented within a regional medical system.[24] These include (1) prehospital catheterization laboratory activation, (2) single call transfer protocol for patients from a non-PCI facility, and (3) ED bypass to transport patients directly to the catheterization laboratory for those presenting by EMS to a PCI-capable hospital, and for transfers from other facilities. In particular, the prehospital activation of catheterization laboratories has been associated with lower short- and long-term mortality in patients presenting with STEMI.[1,8,25] See Section 5.1, "Regional Systems of STEMI Care," for further details.

3.1.2. Initial In-Hospital Assessment of Patients With Confirmed or Suspected ACS

Recommendations for Initial In-Hospital Assessment of Patients With Confirmed or Suspected ACS
Referenced studies that support recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
1	B-NR	1. In patients with suspected ACS, acquisition and interpretation of an ECG within 10 minutes is recommended to help guide patient management.*[1,2]

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Recommendations for Initial In-Hospital Assessment of Patients With Confirmed or Suspected ACS (Continued)		
COR	LOE	Recommendations
1	B-NR	2. In patients with suspected ACS in whom the initial ECG is nondiagnostic, serial 12-lead ECGs should be performed to detect potential ischemic changes, especially when clinical suspicion of ACS is high, symptoms are persistent, or clinical condition deteriorates.*[3]
1	B-NR	3. In patients with suspected ACS, cTn should be measured as soon as possible, preferably using a high-sensitivity cTn (hs-cTn) assay.*[4–7]
1	B-NR	4. In patients with suspected ACS with an initial hs-cTn or cTn that is nondiagnostic, the recommended time intervals for repeat measurements after the initial sample collection (time zero) are 1 to 2 hours for hs-cTn and 3 to 6 hours for conventional cTn assays.*[8–12]

*Adapted from the "2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain."[13]

Synopsis

Chest pain is the second most common presenting complaint to EDs in the United States and has a wide array of potential causes, including ACS.[14] Although most patients with chest pain will not have an ultimate diagnosis of ACS, a missed ACS event has significant implications for the patient's morbidity and mortality. Patients presenting with signs or symptoms of ACS should undergo a history and physical examination, have timely electrocardiographic acquisition and interpretation (Table 3), and assessment of cardiac troponin, because these tests are central to the diagnosis of MI[15] and will guide patient management (Figure 3). A thorough description of the evaluation of patients with suspected ACS is provided in the "2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain."[13] Initial medical treatment should begin immediately for patients with presumed ACS. Urgent echocardiography, which may include an initial point-of-care ultrasound by trained clinicians, is indicated for patients with cardiogenic shock, hemodynamic instability, or for suspected mechanical complications. For patients with suspected STEMI, rapid reperfusion is critical after diagnosis, and further diagnostic testing should not delay cardiac catheterization or fibrinolytic therapy unless it would immediately change patient management. For patients who warrant additional testing to confirm a diagnosis of ACS, selection of the method of assessment may encompass several factors, including clinical history, electrocardiographic findings, cardiac biomarkers, patient preference, and patient exercise capacity. The use of evidence-based clinical decision pathways (CDPs) has been shown to improve outcomes and direct appropriate use of resources.[13] CDPs reduce unnecessary testing in 21% to 43% of patients while maintaining a high negative predictive value for major adverse cardiovascular events (MACE).[16–19]

Recommendation-specific Supportive Text

1. A focused history and rapid evaluation are critical in the assessment of a patient with suspected ACS.[13] Early recognition and initiation of therapy for ACS improves outcomes.[2,20] Rapid electrocardiographic acquisition and interpretation is required for identification of STEMI (Table 3). In patients with NSTE-ACS, the ECG may be normal or demonstrate transient ST-segment elevation (a high-risk finding), ST-segment depression, T-wave inversions, or nonspecific changes. Of note, ST-segment depression in the anteroseptal leads (V1-V3) could indicate an evolving posterior STEMI and therefore should be managed with a high index of suspicion with a posterior lead ECG if warranted (Table 3).[21] Overall, timely acquisition of an ECG is imperative in patients with a goal to obtain and interpret an ECG by a trained clinician within 10 minutes of presentation.[1]
2. An initial nondiagnostic 12-lead ECG does not "rule out" or exclude ACS. Electrocardiographic abnormalities may be dynamic. A nondiagnostic ECG should be compared to prior ECGs, and a repeat ECG should be obtained during the ED course to assess for evolving changes.[3] Right-sided leads should be obtained in patients with a concern for inferior STEMI to evaluate for right ventricular involvement.[22] Assessment for posterior STEMI with an ECG is described in Table 3. The timing of repeat ECGs should be guided by the patient's symptoms, especially recurrent chest pain, and any change in clinical condition.[15] In NCDR ACTION (National Cardiovascular Data Registry and Acute Coronary Treatment and Intervention Outcomes Network), 11% of patients ultimately diagnosed with STEMI had an initial ECG that was nondiagnostic, and 72.4% of those patients had a follow-up ECG diagnostic of STEMI within 90 minutes of their initial ECG.[3]
3. cTn is the biomarker of choice for assessing patients for possible cardiac injury, with hs-cTn assays being preferred. cTn is central to the diagnosis of AMI.[15] Given its high sensitivity and specificity for myocardial injury, cTn (I or T) should be utilized to detect or exclude myocardial injury.[7] In the setting of electrocardiographic evidence of STEMI, reperfusion therapy should not be delayed pending biomarker results. A cTn concentration >99th percentile upper reference limit (a value unique to each assay) is an indicator of myocardial injury.[15,23,24] hs-cTn assays are preferred over conventional cTn assays because the sensitivity and negative predictive values of hs-cTn are greater.[4,15] In addition, the time interval from chest pain onset to detection of hs-cTn is shorter with hs-cTn compared with conventional cTn assays, leading to more rapid "rule in" or "rule out" of ischemia.[25]
4. AMI is characterized by a rising and/or falling pattern of cTn values with at least 1 value above the 99th

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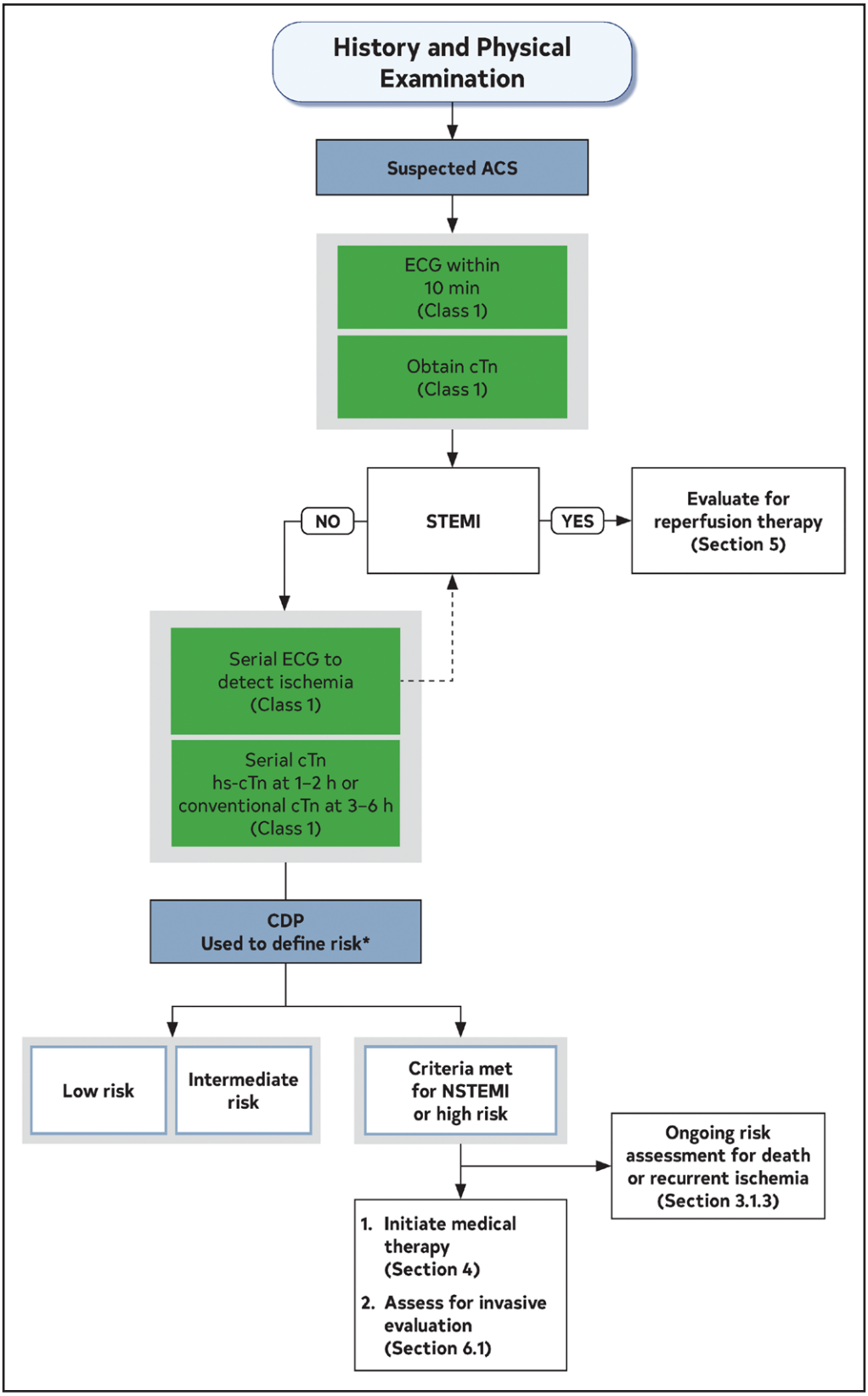
History and Physical Examination
Suspected ACS
ECG within 10 min (Class 1)
Obtain cTn (Class 1)
STEMI
NO
YES
Evaluate for reperfusion therapy (Section 5)
Serial ECG to detect ischemia (Class 1)
Serial cTn hs-cTn at 1–2 h or conventional cTn at 3–6 h (Class 1)
CDP Used to define risk*
Low risk
Intermediate risk
Criteria met for NSTEMI or high risk
Ongoing risk assessment for death or recurrent ischemia (Section 3.1.3)
1. Initiate medical therapy (Section 4)
2. Assess for invasive evaluation (Section 6.1)

Figure 3. Initial Assessment of Patients With Suspected ACS.
Colors correspond to Class of Recommendation in Table 2. *Examples of evidence-based CDPs and definition of low, intermediate, and high risk as defined in the 2021 AHA/ACC/Multisociety Chest Pain Guideline. ACS indicates acute coronary syndromes; CDP, clinical decision pathway; cTn, cardiac troponin; hs-cTn, high-sensitivity cardiac troponin; NSTEMI, non–ST-segment elevation myocardial infarction; and STEMI, ST-segment elevation myocardial infarction. Adapted with permission from Gulati et al.[13] Copyright 2021 American Heart Association, Inc., and American College of Cardiology Foundation.

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percentile upper reference limit and believed caused by myocardial ischemia.[21] With the development of hs-cTn assays enabling detection of circulating cTn at lower concentrations, CDPs using serial testing of hs-cTn at presentation (0 hours) and 1 to 2 hours later provide high negative predictive value, as well as accelerated recognition of myocardial injury.[9,1012] Clinicians should be familiar with both the evidence-based CDPs and the analytical characteristics of the cTn assay (ie, limit of quantification, 99th percentile upper reference limit, and criteria for significant change) used in their practice.[24,26] Men and women may have different cutoff values with hs-cTn assays. With hs-cTn assays, changes in hs-cTn concentration within the normal reference range but below the 99th percentile upper reference limit can signal cardiac ischemia and may warrant further evaluation. CDPs incorporating hs-cTn assays with repeat sampling at 1 or 2 hours from ED arrival with calculation of the change or "delta" hs-cTn can identify patients at very low risk (eg, negative predictive value >99.5%) based on assay-specific diagnostic thresholds.[8,11,27–30] However, when using conventional cTn assays, the sampling timeframe is extended to 3 to 6 hours from ED arrival.[31] cTn may be within normal range early after symptom onset especially when a high-sensitivity assay is not used. When using a CDP that incorporates a single hs-cTn value, the troponin should be obtained at least 3 hours after the onset of symptoms.[32]

3.1.3. Risk Stratification Tools for Patients With STEMI and NSTE-ACS

Synopsis

Substantial variability in short-term mortality and MACE risk exists among patients with ACS. Individual risk assessment can inform discussions with patients and decisions regarding therapeutic interventions. Several risk scores have been developed and validated to help assess a patient's short- and long-term risk in established ACS using commonly available clinical and laboratory variables. Although several risk scores exist,[1–3] the GRACE (Global Registry of Acute Coronary Events) and TIMI (Thrombolysis in Myocardial Infarction) Risk Scores for NSTE-ACS and STEMI (Table 5) are well validated and may be useful for helping to guide some therapeutic decisions (Section 6.1., "Rationale and Timing for a Routine Invasive or Selective Invasive Approach").[4–7] These scores are not to be used as diagnostic tools, because they stratify patient risk in the setting of suspected or confirmed ACS. Risk assessment using the GRACE Risk Score has been found to be superior to subjective physician assessment for the prediction of death or MI in patients with STEMI or intermediate-risk NSTE-ACS.[8] However, there is insufficient evidence that routine use of risk scores in patients hospitalized for STEMI/NSTE-ACS translates into reduced risk of cardiovascular events.[9,10]

Evidence of HF, such as pulmonary congestion detected by physical examination, chest x-ray, or lung ultrasound, is an important risk marker and integral part of the Killip classification (and thereby the GRACE Risk Score and TIMI Risk Score for STEMI) in patients with ACS.[11–15] Similarly, elevated cardiac biomarkers provide prognostic information and also are key elements of the GRACE and TIMI Risk Scores. Higher cTn levels in patients with ACS are associated with an increased risk of death and MACE[16,17] and similarly may be useful for helping to guide some treatment decisions.[4,18] Several other serum or plasma biomarkers may provide additional prognostic information. In particular, natriuretic peptides (including B-type natriuretic peptide and N-terminal pro-

Table 5. Selected Risk Stratification Tools for Patients With ACS

	GRACE Risk Score (2.0)[6,7]	TIMI Risk Score for Unstable Angina/NSTEMI*[4]	TIMI Risk Score for STEMI[5]
Target population	ACS	Unstable angina or NSTEMI	STEMI
Target outcome(s)	In-hospital, 6-mo, 1-y, 3-y, death or death/MI	14-d all-cause death, MI, or urgent revascularization	30-d all-cause death
Variables used	In-hospital risk score	Age ≥65 y	Age (65-74 y/≥75 y) (2-3 points)
	Age	≥3 risk factors for CAD	Killip class II-IV (2 points)*
	Killip class	Known coronary stenosis (≥50%)	Systolic blood pressure (<100 mm Hg, 3 points)
	Systolic blood pressure	ST-segment deviation ≥0.5 mm	Heart rate >100 bpm (2 points)
	Heart rate	≥2 anginal events in prior 24 h	Anterior ST-segment elevation or LBBB (1 point)
	ST-segment deviation	Aspirin use in prior 7 d	Diabetes/hypertension/angina (1 point)
	Cardiac arrest on admission	Elevated cardiac biomarkers (CK-MB or troponin)	Weight (<67 kg, 1 point)
	Serum creatinine		Time to treatment >4 h (1 point)
	Elevated cardiac biomarkers		

*Score 1 point for each characteristic that is present.

ACS indicates acute coronary syndromes; bpm, beats per minute; CAD, coronary artery disease; CK-MB, creatine kinase-myocardial band; GRACE, Global Registry of Acute Coronary Events; LBBB, left bundle branch block; MI, myocardial infarction; NSTEMI, non–ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; and TIMI, Thrombolysis in Myocardial Infarction.

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B-type natriuretic peptide) may identify those patients with ACS at increased risk of death, HF, and recurrent MACE.[19,20]

Early recognition of cardiogenic shock in patients presenting with ACS on FMC by EMS or ED providers is the key to initial triage and risk stratification.[21] Cardiogenic shock related to AMI is present in 7% to 10% of the ACS population and carries a high mortality rate.[22] Early and rapid revascularization for cardiogenic shock related to AMI is associated with increased survival, and triage to a PCI-capable hospital and ideally to hospitals providing advanced therapies (eg, mechanical circulatory support [MCS]) is preferred (Section 8.1, "Revascularization in ACS With Cardiogenic Shock" and Section 8.2, "MCS in Patients With ACS and Cardiogenic Shock"). Several scales are available to determine the severity of shock, and observational data have shown associations between severity as assessed by these scales and outcomes.[23]

3.2. Management of Patients Presenting With Cardiac Arrest

Recommendations for Management of Patients Presenting With Cardiac Arrest
Referenced studies that support recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
1	C-LD	1. Patients with cardiac arrest and STEMI who have been resuscitated should preferentially be transferred by EMS to a PPCI-capable center.[1,2]
1	B-NR	2. Patients who have been resuscitated after cardiac arrest and are noncomatose or who are comatose with favorable prognostic features and with evidence of STEMI, should undergo PPCI to improve survival.[3–7]
2b	C-LD	3. In patients with cardiac arrest who are comatose, have unfavorable prognostic features, and evidence of STEMI, PPCI may be reasonable after individualized assessment.[4,7]
3: No Benefit	A	4. In resuscitated patients who are comatose after cardiac arrest, electrically and hemodynamically stable, and without evidence of STEMI, immediate angiography is not recommended due to lack of benefit.[8–14]

Synopsis

Approximately 10% of patients with STEMI transferred by EMS to the hospital are estimated to have an out-of-hospital cardiac arrest.[15] Early recognition of STEMI in resuscitated patients and direct transfer to a PCI-capable center is associated with improved survival.[1,2] Survival-to-hospital discharge in the patient who is comatose with out-of-hospital cardiac arrest is <10% regardless of etiology.[16] Those with a witnessed arrest and a shockable rhythm have improved survival. Outcomes for patients with STEMI who are awake after resuscitated cardiac arrest are comparable to patients with STEMI who were not in cardiac arrest.[3] For this reason, patients with cardiac arrest who have achieved return of spontaneous circulation (ROSC) and are awake with STEMI on ECG are candidates for PPCI. However, care should be individualized in the comatose patient with rapid assessment of the patient's clinical features and cardiac arrest characteristics before proceeding with invasive angiography.[17–19] In contrast, patients who are stable without ST-segment elevation after out-of-hospital cardiac arrest do not require immediate coronary angiography. Coronary angiography can be deferred pending further risk stratification.[8–13]

Recommendation-Specific Supportive Text

1. Observational studies have shown an association between triage of out-of-hospital cardiac arrest patients to a PCI-capable facility with improved outcomes.[1,2,15] Data from the CARES (Cardiac Arrest Registry to Enhance Survival) registry showed that transfer to a PCI-capable center was associated with improved survival in patients with cardiac arrest and STEMI on ECG. EMS should preferentially transfer patients who are comatose after cardiac arrest, have achieved ROSC, and have STEMI on the ECG to a PPCI center.[2] Although the ARREST (Advanced Reperfusion Strategies for Patients With Out of Hospital Cardiac Arrest and Refractory Ventricular Fibrillation) trial did not show a benefit in triaging patients to primary cardiac arrest centers, this study evaluated patients without STEMI on the ECG.[20]
2. Nearly one-third of patients with cardiac arrest and STEMI on ECG have normal neurologic status on presentation to the ED.[3] Being alert or with partial/minimal neurologic response on presentation with STEMI after cardiac arrest is an independent predictor of survival. Observational studies have demonstrated comparable survival of the awake patient with STEMI with cardiac arrest to those patients with STEMI without cardiac arrest.[3] For this reason, patients with STEMI who have achieved ROSC and are awake should undergo PPCI (Section 5.2.1, "PPCI in STEMI").
3. In patients who are comatose after cardiac arrest and have achieved ROSC, but have STEMI on the ECG, an individualized patient assessment for survival and futility is essential before proceeding with PCI. Observational data have identified poor prognostic features that have been validated and incorporated into risk scores for this population. These include unwitnessed arrest, no bystander cardiopulmonary resuscitation, nonshockable rhythm, cardiopulmonary resuscitation >30 minutes, time to ROSC >30 minutes, arterial pH <7.2, lactate >7 mmol/L, age >85 years, and end-stage renal

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disease on dialysis.[4,21–30] Although these data suggest a lack of clear benefit for invasive therapies for patients with STEMI and cardiac arrest who have features indicating an unfavorable neurologic prognosis,[4,7] this has not been validated in prospective trials. However, for those patients with favorable prognostic features, PPCI is associated with greater survival.[4,7,27]

4. Six contemporary trials[9–14] have evaluated the role of emergency angiography in patients who remain comatose after cardiac arrest, do not have ST-segment elevation on a 12-lead ECG, and are electrically and hemodynamically stable. These studies consistently demonstrated a lack of benefit to early angiography when compared with delayed or no angiography in the study population with comparable in-hospital and 6-month survival, as well as neurologic recovery.[31] The relative utility of delayed coronary angiography in this population is uncertain.

4. STANDARD MEDICAL THERAPIES FOR STEMI AND NSTE-ACS

4.1. Oxygen Therapy

Recommendations for Oxygen Therapy
Referenced studies that support recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
1	C-LD	1. In patients with ACS and confirmed hypoxia (oxygen saturation <90%), supplemental oxygen to increase oxygen saturations to ≥90% is recommended to improve myocardial oxygen supply and decrease anginal symptoms.[1]
3: No Benefit	A	2. In patients with ACS and oxygen saturations ≥90%, routine administration of supplemental oxygen is not recommended because it does not improve cardiovascular outcomes.[2–4]

Synopsis

Supplemental oxygen has historically been administered as part of routine care in the management of patients with suspected ACS, although evidence to suggest clinical benefit in the absence of hypoxia has been lacking.[5] Randomized trials that have enrolled patients with MI and without hypoxia have not demonstrated any clinical benefit from routine use of supplemental oxygen (≥6 L/min)[2–4,6] and have raised some concerns that it may increase myocardial injury by increasing vasoconstriction and increasing oxidative stress.[3]

Recommendation-Specific Supportive Text

1. Use of supplemental oxygen may provide benefit to patients who present with hypoxia (peripheral capillary oxygen saturations <90%), including those who present with acute or chronic conditions that require the need for supplemental oxygen to achieve an oxygen saturation ≥90%. A systematic review and meta-analysis of RCTs in acutely ill adults from various causes without hypoxia suggested worse short- and long-term mortality with liberal compared with conservative administration of supplemental oxygen.[7] These studies were unable to define the optimal oxygen saturation target range to minimize potential harm and maximize clinical benefit. The observed relationship between oxygenation and outcomes appears to be U-shaped with the lowest mortality rate described for those patients with an Spo_2 of 94% to 96% at presentation.[8]
2. Several randomized trials have now demonstrated a lack of cardiovascular benefit with routine use of supplemental oxygen in patients presenting with known or suspected AMI and oxygen saturations ≥90%. Although exclusion criteria varied among studies, patients with a home oxygen requirement, active bronchospasm requiring supplemental oxygen, or with cardiac arrest at presentation were excluded.[2–4,6] The AVOID (Air Versus Oxygen in ST-Segment-Elevation Myocardial Infarction) trial investigated the effects of supplemental oxygen (8 L/min) in patients with STEMI and oxygen saturations ≥94% and demonstrated a lack of benefit with routine supplemental oxygen, including a possible increase in myocardial injury and infarct size.[3] DETO2X-AMI (Efficacy and Outcome Study of Supplemental Oxygen Treatment in Patients With Suspected Myocardial Infarction) evaluated the use of routine supplemental oxygen (6 L/min) in 6629 patients with suspected MI and an oxygen saturation ≥90%.[2] The use of supplemental oxygen did not reduce all-cause mortality at 1 year and did not reduce rehospitalization with MI.[2,9] A consistent lack of clinical benefit was seen in the study for those with lower baseline oxygen saturations (90%-94%).[10]

4.2. Analgesics

Synopsis

Patients presenting with known or suspected ACS often experience chest pain or other uncomfortable symptoms. Rapid and effective pain relief remains an important treatment goal to prevent sympathetic activation and adverse clinical sequelae (Table 6). Analgesic therapies may provide symptomatic relief, but they have not been shown to improve clinical outcomes in patients with ACS.[1,2] Nitrates and opiate medications remain effective treatment options for management of pain in ACS but should be thoughtfully utilized to prevent potential harm.[3–6] In particular, rapid coronary revascularization should be pursued for patients with ongoing ischemic symptoms that are not relieved with nitrates, and opiates should not be

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Table 6. Analgesic Treatment Options for Cardiac Chest Pain

Medication	Route	Suggested Dosing	Considerations
Nitroglycerin*	SL (tablets, spray)	0.3 or 0.4 mg every 5 min as needed up to a total of 3 doses	Use in hemodynamically stable patients with SBP ≥90 mm Hg.
Nitroglycerin*	IV	Start at 10 µg/min and titrate to pain relief and hemodynamic tolerability.	Consider for persistent anginal pain after oral nitrate therapy, or if ACS is accompanied by hypertension or pulmonary edema.[20–22] Avoid use in suspected RV infarction, SBP <90 mm Hg or a change in SBP >30 mm Hg below baseline. Tachyphylaxis may occur after approximately 24 h.
Morphine	IV	2-4 mg; may repeat if needed every 5-15 min. Doses up to 10 mg may be considered.	Use for relief of pain that is resistant to other maximally tolerated anti-ischemic medications. May delay the effects of oral P2Y12 therapy.[7,9–12] Monitor closely for adverse effects.
Fentanyl	IV	25-50 µg; may repeat if needed. Doses up to 100 µg may be considered.	Use for relief of pain that is resistant to other maximally tolerated anti-ischemic medications. May delay the effects of oral P2Y12 therapy.[8] Monitor closely for adverse effects.

*Nitrates should not be administered after recent PDE5 inhibitor use. Avoid use of nitrates/nitroglycerin within 12 h of avanafil, 24 h of sildenafil/vardenafil, or 48 h of tadalafil.[23–25]

ACS indicates acute coronary syndromes; PDE5, phosphodiesterase-5 inhibitor; RV, right ventricular; SBP, systolic blood pressure; and SL, sublingual.

used solely to mask these symptoms. Concerns have also been raised that the use of opiates may delay gastric and intestinal absorption of orally administered P2Y12 inhibitors, thereby delaying their pharmacodynamic effects in patients undergoing PCI.[7–10] However, the clinical relevance of these pharmacodynamic findings remains disputed.[11–14] Use of nonaspirin nonsteroidal anti-inflammatory drugs should be avoided for management of suspected or known ischemia pain whenever possible.[15–17] Use of nonsteroidal anti-inflammatory drugs is associated with increased risk of MACE in patients with and without prior cardiac disease, with no documented benefit to support routine use in patients with ACS.[15–19]

4.3. Antiplatelet Therapy

4.3.1. Aspirin

Recommendation for Aspirin Referenced studies that support recommendations are summarized in the Evidence Table.		
COR	**LOE**	**Recommendation**
1	A	1. In patients with ACS, an initial oral loading dose of aspirin, followed by daily low-dose aspirin, is recommended to reduce death and MACE.[1–5]

Synopsis

Aspirin has long been considered an integral part of antiplatelet therapy to prevent recurrent atherothrombotic events among patients with ACS.[1–3,6] Aspirin reduces the incidence of vascular death after AMI,[3] and in secondary prevention trials (that include patients after MI), it reduces the occurrence of vascular and coronary events, including MI and stroke.[2] Although aspirin use after ACS was traditionally considered lifelong, a strategy of aspirin discontinuation, rather than P2Y12 inhibitor discontinuation, may now be considered in the maintenance phase after 1 to 3 months in selected patients to reduce risk of bleeding (Section 11.1, "DAPT Strategies in the First 12 Months Postdischarge"). Aspirin discontinuation after 1 to 4 weeks after PCI is also appropriate for patients on a full-dose anticoagulant in combination with continued use of a P2Y12 inhibitor (Section 11.1.1, "Antiplatelet Therapy in Patients on Anticoagulation Postdischarge"). For patients in whom a history of aspirin hypersensitivity is reported, aspirin desensitization is preferred whenever possible to allow for initial use of dual antiplatelet therapy.[7–9] The use of a P2Y12 inhibitor is recommended in all patients with ACS regardless of whether they have a history of aspirin hypersensitivity, but should be administered with a loading dose as early as possible for those patients unable to take aspirin at presentation.

Recommendation-Specific Supportive Text

1. Aspirin should be initiated with a loading dose (162-325 mg) in patients with ACS without an absolute contraindication as soon as possible on presentation irrespective of final management strategy (invasive or noninvasive), followed by a daily maintenance dose (Table 7 in Section 4.3.2, "Oral P2Y12 Inhibitors During Hospitalization"). In patients who cannot take oral medication, rectal or intravenous (where available) administration are options for administration. Current evidence supports the use of uncoated low-dose aspirin (75-100 mg) for daily maintenance therapy. The 75 to 100 mg daily dose of aspirin exceeds the minimal effective dose required for platelet thromboxane A_2 suppression, allowing for some interindividual variability in drug response.[10] Among patients with ACS referred for an invasive strategy, continued use of full-dose aspirin (300-325 mg daily) for 30 days (following an initial loading dose) was not superior to low-dose aspirin (75-100 mg daily) for reduction of MACE but was associated with increased minor and gastrointestinal bleeding.[4] In an open-label

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Table 7. Dosing Considerations for Oral Antiplatelet Therapy in Patients With ACS

Agent	Setting	Dosing Considerations
Aspirin	NSTE-ACS or STEMI	Loading dose 162-325 mg orally. Aspirin (nonenteric coated) should be chewed, when possible, to achieve faster onset of antiplatelet action. Loading dose should be administered for patients already on aspirin therapy. Maintenance dose 75-100 mg orally daily (nonenteric coated)
Clopidogrel	NSTE-ACS or STEMI without fibrinolytic	Loading dose 300 or 600 mg orally Maintenance 75 mg orally daily
	STEMI with fibrinolytic	Loading dose 300 mg orally if age ≤75 y; Initial dose 75 mg orally if age >75 y Maintenance 75 mg orally daily
Prasugrel	NSTE-ACS or STEMI without fibrinolytic, and undergoing PCI	Loading dose 60 mg orally Maintenance dose 10 mg orally daily if body weight ≥60 kg and age <75 y Maintenance dose 5 mg orally daily if body weight <60 kg or age ≥75 y (use caution)
Ticagrelor	NSTE-ACS or STEMI without fibrinolytic	Loading dose 180 mg orally Maintenance dose 90 mg orally twice daily

NSTE-ACS indicates non–ST-segment elevation acute coronary syndromes; PCI, percutaneous coronary intervention; and STEMI, ST-segment elevation myocardial infarction.

RCT of patients with established atherosclerotic cardiovascular disease (ASCVD), 35% of whom had a previous MI, no significant differences were observed in MACE or major bleeding for patients treated with 81 mg of aspirin daily and those treated with 325 mg daily, although a high degree of crossover between study arms was observed.[5] Together, these data support the use of low-dose aspirin (75-100 mg daily) for maintenance therapy. Based on an association between aspirin dosing and outcomes in a *post hoc* analysis of the PLATO (Platelet Inhibition and Patient Outcomes) trial, aspirin doses of ≤100 mg daily should always be used in patients treated with ticagrelor.[11]

4.3.2. Oral P2Y12 Inhibitors During Hospitalization

Recommendations for Oral P2Y12 Inhibitors During Hospitalization
Referenced studies that support recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
All Patients With ACS (STEMI and NSTE-ACS)		
1	A	1. In patients with ACS, an oral P2Y12 inhibitor should be administered in addition to aspirin to reduce MACE.[1–5]
3: Harm	B-R	2. In patients with a history of stroke or transient ischemic attack, prasugrel should not be administered because of worse net clinical outcomes.*†[4]
In-Hospital Management in Patients With NSTE-ACS		
1	B-R	3. In patients with NSTE-ACS undergoing PCI, prasugrel or ticagrelor is recommended to reduce MACE and stent thrombosis.[4–6]
1	B-R	4. In patients with NSTE-ACS who are managed without planned invasive evaluation, ticagrelor is recommended to reduce MACE.[5,7]
1	B-R	5. In patients with NSTE-ACS, clopidogrel is recommended to reduce MACE when prasugrel or ticagrelor are unavailable, cannot be tolerated, or are contraindicated.[1]

Recommendations for Oral P2Y12 Inhibitors During Hospitalization (Continued)

COR	LOE	Recommendations
2b	B-NR	6. In patients with NSTE-ACS planned for an invasive strategy with timing of angiography anticipated to be >24 hours, upstream treatment with clopidogrel or ticagrelor may be considered to reduce MACE.[1,5,8]
In-Hospital Management in Patients With STEMI		
1	B-R	7. In patients with STEMI managed with PPCI, prasugrel or ticagrelor should be administered to reduce MACE and stent thrombosis.[4,5,9,10]
1	C-LD	8. In patients with STEMI managed with PPCI, clopidogrel is recommended to reduce MACE and stent thrombosis when prasugrel or ticagrelor are unavailable, cannot be tolerated, or are contraindicated.[11]
1	A	9. In patients with STEMI managed with fibrinolytic therapy, clopidogrel should be administered concurrently to reduce death and MACE.[2,3]

*Modified from the "2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization"[12] and the

†"2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline for the Management of Patients With Chronic Coronary Disease."[13]

Synopsis

Oral inhibitors of the platelet P2Y12 receptor antagonize adenosine diphosphate–mediated activation of platelets. Across the spectrum of ACS, the addition of a P2Y12 inhibitor to aspirin significantly reduces platelet aggregation and has been shown to reduce the incidence of recurrent MACE but with an increased risk of bleeding.[1–5,9,10] In addition to receiving aspirin, patients with ACS should therefore be treated with a loading dose of an oral P2Y12 inhibitor followed by daily dosing (Table 7). The selection of the specific type of oral P2Y12 inhibitor should involve several considerations, including the patient's anticipated management strat-

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egy and their risk of bleeding (Figure 4).[1–5,9,10] Clinically available oral P2Y12 inhibitors include clopidogrel, prasugrel, and ticagrelor. Clopidogrel is the least potent oral P2Y12 inhibitor and requires more time to reach its maximal platelet inhibition after a loading dose, because it requires biotransformation in the liver to form its active metabolite. Pharmacodynamic variability in response in clopidogrel has been well described,[14,15] and hyporesponders may be at increased risk of MACE and stent thrombosis when treated with clopidogrel after PCI.[16,17] Ticagrelor and prasugrel are more potent than clopidogrel and achieve more rapid onset of inhibition of platelet activation but with increased risk of bleeding compared with clopidogrel. Of note, ticagrelor may cause subjective transient dyspnea in approximately 10% to 15% of patients after ACS.[5] The topic of duration of dual antiplatelet therapy is addressed in Section 11.1, "DAPT Strategies in the First 12 Months Postdischarge."

Recommendation-Specific Supportive Text

1. Several trials have demonstrated the clinical benefit of oral P2Y12 inhibitors in ACS for reducing MACE but with increased risk of bleeding. In randomized placebo-controlled trials in both NSTE-ACS and STEMI, the addition of clopidogrel to aspirin reduced risk of MACE irrespective of management strategy.[1–3] In patients with STEMI treated with fibrinolytic therapy, the addition of clopidogrel to aspirin reduces 30-day MACE, including recurrent MI, and improves survival.[2,3] Moreover, in randomized trials, the use of prasugrel and ticagrelor further reduced risk of MACE, as well as stent thrombosis, when compared with clopidogrel in patients with STEMI (not receiving concurrent fibrinolytic therapy) or NSTE-ACS.[4,5] The benefits of oral P2Y12 inhibitors have also been demonstrated in patients after coronary artery bypass graft (CABG) surgery.[18–21] Guidance on dosing interruption for patients referred for CABG is in Table 8. Duration of administration after CABG is described in Section 11.1, **"**DAPT Strategies in the First 12 Months Postdischarge."
2. In a secondary analysis of the randomized, double-blind TRITON-TIMI 38 (Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel–Thrombolysis in Myocardial Infarction) of prasugrel versus clopidogrel in addition to aspirin among patients with ACS, subgroup analyses using an outcome of net clinical benefit (MACE events plus bleeding) demonstrated net harm with prasugrel versus clopidogrel among patients with previous transient ischemic attack or stroke.[4] Dose reduction of prasugrel should be considered in patients ≥75 years of age and in those with a body weight <60 kg (Table 7).
3. The randomized, double-blind TRITON-TIMI 38 and PLATO trials demonstrated that prasugrel (TRITON-TIMI 38) or ticagrelor (PLATO) reduced the rate of the composite endpoint of

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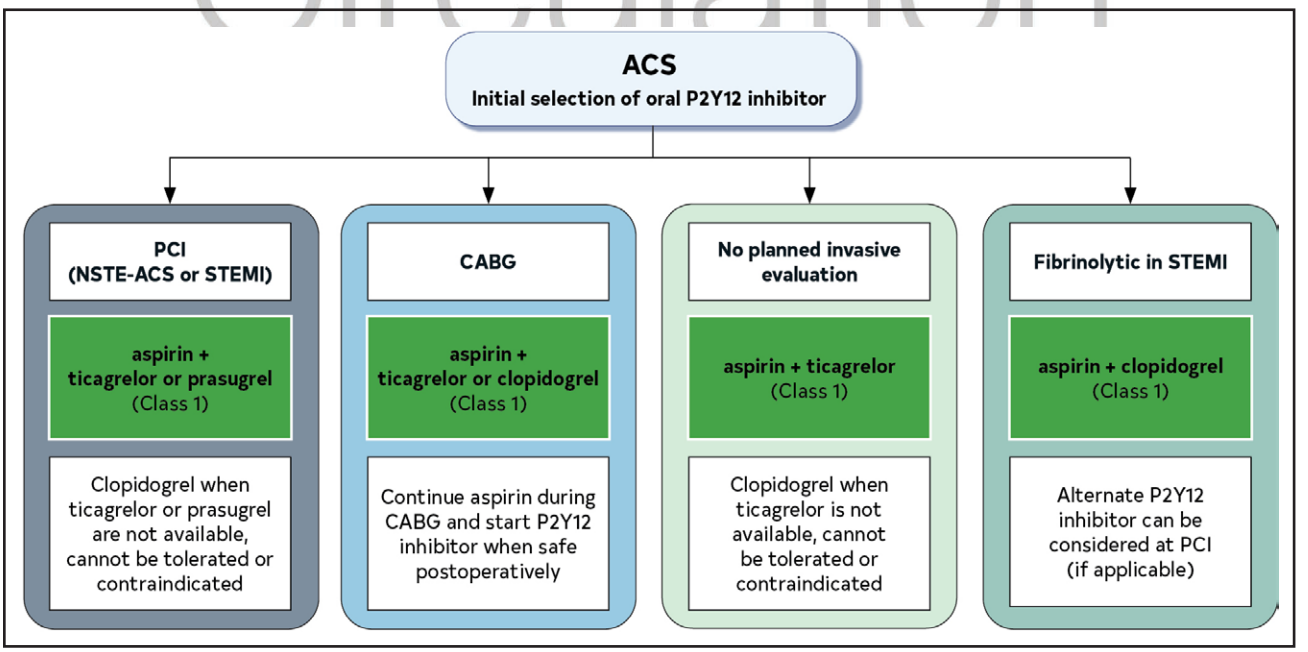
ACS
Initial selection of oral P2Y12 inhibitor
PCI (NSTE-ACS or STEMI)
aspirin + ticagrelor or prasugrel (Class 1)
Clopidogrel when ticagrelor or prasugrel are not available, cannot be tolerated or contraindicated
CABG
aspirin + ticagrelor or clopidogrel (Class 1)
Continue aspirin during CABG and start P2Y12 inhibitor when safe postoperatively
No planned invasive evaluation
aspirin + ticagrelor (Class 1)
Clopidogrel when ticagrelor is not available, cannot be tolerated or contraindicated
Fibrinolytic in STEMI
aspirin + clopidogrel (Class 1)
Alternate P2Y12 inhibitor can be considered at PCI (if applicable)

Figure 4. Initial Choice of P2Y12 Inhibitor in Patients Not Requiring an Oral Anticoagulant.
Colors correspond to Class of Recommendation in Table 2.
ACS indicates acute coronary syndromes; ASA, aspirin; CABG, coronary artery bypass grafting; NSTE-ACS, non–ST-segment elevation ACS; PCI, percutaneous coronary intervention; and STEMI, ST-segment elevation myocardial infarction.

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Table 8. Management of Oral P2Y12 Inhibitors for Patients Who Require CABG Surgery*

Clopidogrel	Elective CABG: Interrupt for 5 d before surgery. Urgent CABG: Interruption for at least 24 h (ideally) and proceeding earlier than 5 d may be reasonable.
Prasugrel	Elective CABG: Interrupt for 7 d before surgery. Urgent CABG: Interruption for at least 24 h (ideally) and proceeding earlier than 7 d may be reasonable.
Ticagrelor	Elective CABG: Interrupt for 3-5 d before surgery. Urgent CABG: Interruption for at least 24 h (ideally) and proceeding earlier than 5 d may be reasonable.

*For all patients, oral P2Y12 inhibitor should be resumed after surgery when bleeding risk not excessive (typically 24-72 hours).
CABG indicates coronary artery bypass grafting.

cardiovascular death, MI, or stroke by 16% to 20% when compared with clopidogrel, as well as reduced the risk of stent thrombosis.[4,5] In the PLATO trial, a nominal reduction in all-cause death with ticagrelor compared with clopidogrel was also observed.[5] In TRITON-TIMI 38, the P2Y12 inhibitor (prasugrel or clopidogrel) was only administered in patients with NSTE-ACS once the anatomy was deemed suitable for PCI. In the PLATO trial, 72% were managed with a planned invasive strategy and results in the invasively managed population were highly consistent with the overall trial for reducing MACE, as well as cardiovascular and all-cause death individually.[6] Both prasugrel and ticagrelor increase the risk of non-CABG major bleeding compared with clopidogrel.[4,5] Prasugrel has been shown to increase life-threatening bleeds.[4] Limited data exist to compare the efficacy and safety of prasugrel versus ticagrelor head-to-head. One open-label randomized trial reported a lower rate of MACE with similar bleeding with prasugrel administered at the time of PCI compared with ticagrelor used as upstream therapy in patients with ACS undergoing invasive evaluation.[22]

4. The randomized, double-blind PLATO trial of ticagrelor versus clopidogrel included patients with ACS managed with or without a planned invasive strategy. Among the 28% of patients (n=5216) who were managed without a planned invasive strategy, a 15% reduction was observed in the primary endpoint of vascular death, MI, or stroke with ticagrelor versus clopidogrel that was highly consistent with the 16% reduction in MACE in the overall trial. Similarly, the findings for bleeding were consistent with the overall trial result.[5,7]
5. In the randomized, double-blind, placebo-controlled CURE (Clopidogrel in Unstable Angina to Prevent Recurrent Events) trial, among patients with NSTE-ACS receiving aspirin and who were medically managed or underwent revascularization, the administration of clopidogrel significantly reduced the composite of cardiovascular death, MI, or stroke.[1] Although prasugrel and ticagrelor further reduce major cardiovascular events compared with clopidogrel in patients with ACS undergoing PCI, these more potent agents also further increase the risk of bleeding.[4,5] Clopidogrel is an effective alternative P2Y12 inhibitor for use in patients with high bleeding risk or contraindications to prasugrel or ticagrelor. In an open-label trial with a high crossover rate among older patients with ACS undergoing PCI, patients treated with clopidogrel had a similar rate of ischemic events and less bleeding compared with ticagrelor.[23] Significant interpatient variability in the pharmacodynamic response to clopidogrel has been described.[15]
6. In a prospective substudy among the patients who underwent PCI (n=2658) in the CURE trial, those who were pretreated with clopidogrel (median 6 days) prior to PCI had a significantly lower rate of MACE both before PCI and by 30 days.[8] Clopidogrel is a prodrug that requires metabolism by the cytochrome P450 enzyme system to form its active metabolite and therefore may require several hours before significant antiplatelet effect is observed following a loading dose. A meta-analysis of trials of clopidogrel in patients with ACS undergoing PCI found that pretreatment with clopidogrel significantly reduced the risk for 30-day cardiovascular death or MI.[11] However, less is known regarding the need for pretreatment in the era of more potent P2Y12 inhibitors with more rapid onset of antiplatelet action. In a randomized trial of prasugrel pretreatment versus administration at the time of PCI, pretreatment (median of only 4.4 hours) did not improve ischemic outcomes, but significantly increased bleeding.[24] In the PLATO trial, knowledge of coronary anatomy prior to administration of the study drug was not required; however, upstream use of ticagrelor was not specifically compared with a strategy of administration at time of PCI. Therefore, it remains unknown whether a benefit exists for administration of ticagrelor prior to PCI in patients with NSTE-ACS. For this reason, routine pretreatment in patients undergoing an early invasive management strategy (<24 hours) is not supported by clinical trial data. However, it may be reasonable to consider pretreatment with clopidogrel or ticagrelor in patients undergoing an invasive management strategy with the timing of angiography anticipated to be ≥24 hours from administration of the loading dose.

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7. The clinical efficacy of prasugrel and ticagrelor compared with clopidogrel in TRITON-TIMI 38 and the PLATO trial was consistent in patients undergoing PPCI or delayed (ie, secondary) PCI after initial therapy for STEMI.[4,5] In the subgroup of patients with STEMI in TRITON-TIMI 38 (n=3534), prasugrel significantly reduced MACE by 21% and stent thrombosis by 42% at 15 months without a clear excess in bleeding.[9] In the PLATO trial, compared with clopidogrel, treatment of patients with STEMI undergoing PPCI (n=7544) with ticagrelor was associated with a consistent trend toward reduction in cardiovascular death, recurrent MI, or stroke, as well as a significant reduction in stent thrombosis and an 18% reduction in all-cause death.[10] Both TRITON-TIMI 38 and the PLATO trial permitted study drug administration prior to the initial angiogram for patients with STEMI undergoing primary PCI. In a separate randomized trial in PPCI for STEMI, allocation to prehospital ticagrelor or hospital administration did not improve the primary endpoint of coronary reperfusion prior to the PCI.[25] However, upstream administration of ticagrelor was associated with a reduction in stent thrombosis with similar bleeding between treatment groups. Registry data have also not shown clear clinical benefit for preloading a P2Y12 inhibitor in patients with STEMI,[26] but a meta-analysis that included patients with STEMI showed that clopidogrel pretreatment was associated with a lower risk for MACE without an increase in bleeding.[27]
8. Clopidogrel is effective for prevention of stent thrombosis and early recurrent ischemic events in patients with STEMI undergoing PCI.[11] As in patients with NSTE-ACS, in patients with STEMI undergoing PPCI, prasugrel and ticagrelor reduce the risk of recurrent MACE compared with clopidogrel.[9,10] Administration of clopidogrel is an alternative to prasugrel or ticagrelor in patients with STEMI who are at high bleeding risk or have other contraindications to those agents.
9. In the CLARITY (Clopidogrel as Adjunctive Reperfusions Therapy)-TIMI 28 trial, addition of clopidogrel to aspirin in patients with STEMI who were <75 years of age and received fibrinolytic therapy reduced the odds of an occluded infarct-related artery at angiography, as well as the composite of cardiovascular death, recurrent MI, or recurrent ischemia requiring urgent revascularization by 30 days.[2] In the randomized, placebo-controlled COMMIT (Clopidogrel and Metoprolol in Myocardial Infarction Trial) study among patients with suspected MI (93% STEMI, 54% fibrinolytic-treated) receiving aspirin, clopidogrel 75 mg/day (without a loading dose), significantly lowered the risk of the composite endpoint of death, reinfarction, or stroke, as well as the endpoint of mortality alone, with a consistent pattern in the subgroup treated with fibrinolytic.[3] No significant excess was observed in bleeding with clopidogrel versus placebo. Based on the design of these 2 trials, when administered concurrently with fibrinolytic as the reperfusion strategy, clopidogrel is recommended to be administered with a loading dose (300 mg, then 75 mg daily) for patients <75 years of age and starting without a loading dose (75 mg daily) for patients ≥75 years of age. In patients treated with a fibrinolytic agent who are undergoing subsequent PCI, either clopidogrel or ticagrelor (age <75 years, within 24 hours after a fibrinolytic agent) or prasugrel (>24 hours after a fibrinolytic agent) are alternatives to support PCI.[9–12,28] In a trial of 3799 patients with STEMI who were treated with a fibrinolytic agent, 89% of whom also received clopidogrel at the time of a fibrinolytic agent, randomization to ticagrelor administered at a median of 11.4 hours (interquartile range, 5.8-18.2 hours) after fibrinolytic therapy was noninferior to clopidogrel with respect to major bleeding.[28]

4.3.3. Intravenous P2Y12 Inhibition

Recommendation for Intravenous P2Y12 Inhibition
Referenced studies that support recommendations are summarized in the Evidence Table.

COR	LOE	Recommendation
2b	B-R	1. Among patients with ACS undergoing PCI who have not received a P2Y12 inhibitor, intravenous cangrelor may be reasonable to reduce periprocedural ischemic events.*[1–4]

*Reproduced from the "2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization."[5]

Synopsis

Cangrelor is a direct-acting, intravenous antagonist of the P2Y12 receptor characterized by rapid and potent platelet inhibitory effects with restoration of platelet function occurring within 1 hour of drug discontinuation.[6] These pharmacological properties may be particularly beneficial in clinical scenarios wherein absorption of orally administered P2Y12 inhibitors is impaired or not possible, as well as in patients requiring CABG or other surgery early after PCI when prolonged discontinuation of a P2Y12 inhibitor may not be safe.[7] The safety and efficacy of cangrelor has been compared with clopidogrel or placebo in 3 RCTs involving patients who are P2Y12 inhibitor-naïve and undergoing PCI for stable or acute indications.[1–3] In a patient-level pooled analysis of these studies, cangrelor administered during PCI significantly reduced periprocedural ischemic events albeit at the expense of more frequent minor bleeding.[4] The safety and efficacy of cangrelor versus ticagrelor or prasugrel with respect to ischemic events have not been established. The transition from intravenous to oral P2Y12 inhibition is an important consideration to ensure adequate platelet inhibition on completion of cangrelor infusion (Table 9).[8]

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Table 9. Transition From Intravenous Cangrelor Infusion to Oral P2Y12 Inhibitor

Oral P2Y12 inhibitor	Loading Dose	Timing of Loading Dose Administration
Clopidogrel	600 mg	Immediately after discontinuation of cangrelor
Prasugrel	60 mg	Immediately after discontinuation of cangrelor
Ticagrelor	180 mg	At any time during or immediately after discontinuation of cangrelor

Recommendations in table obtained from US Food and Drug Administration labeling for cangrelor.[8]

Recommendation-Specific Supporting Text

1. CHAMPION PHOENIX (A Clinical Trial Comparing Cangrelor to Clopidogrel Standard Therapy in Subjects Who Require PCI) examined the effect of cangrelor versus clopidogrel in patients undergoing PCI for acute or stable coronary syndromes.[2] Cangrelor was administered as an intravenous bolus prior to PCI followed by an infusion for at least 2 hours or for the duration of the procedure, whichever was longer. In the control arm, clopidogrel was administered as a 600- or 300-mg loading dose immediately before or after PCI. At 48 hours, the primary endpoint of all-cause death, MI, ischemia-driven revascularization, or stent thrombosis was significantly reduced with cangrelor with similar effects observed among those presenting with NSTE-ACS (n=2810) or STEMI (n=1991). These results contrast with the earlier neutral findings from the CHAMPION PLATFORM (Cangrelor Versus Standard Therapy to Achieve Optimal Management of Platelet Inhibition) trial and CHAMPION PCI (A Clinical Trial to Demonstrate the Efficacy of Cangrelor), which compared cangrelor with placebo and clopidogrel, respectively.[1,3] Differences across trials in the timing of clopidogrel administration and definitions of MI and stent thrombosis may in part account for variability in the incidence of ischemic events and observed treatment effect. In a pooled analysis of these trials, cangrelor was associated with a significant reduction in periprocedural ischemic events compared with control with no evidence of heterogeneity across types of ACS presentations.[4]

4.3.4. Intravenous Glycoprotein IIb/IIIa Inhibitors

Recommendations for Intravenous Glycoprotein IIb/IIIa Inhibitors Referenced studies that support recommendations are summarized in the Evidence Table.		
COR	**LOE**	**Recommendations**
2a	**C-LD**	1. In patients with ACS undergoing PCI with large thrombus burden, no-reflow, or slow flow, adjunctive use of an intravenous or intracoronary glycoprotein IIb/IIIa inhibitor is reasonable to improve procedural success and reduce infarct size.*[1,2]
3: Harm	**B-R**	2. In patients with ACS, glycoprotein IIb/IIIa inhibitors should not be administered routinely due to lack of ischemic benefit and increased risk of bleeding.[3–5]

*Adapted from the "2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization."[6]

Synopsis

Glycoprotein IIb/IIIa receptor inhibitors are parenterally administered drugs that block platelet aggregation by preventing platelet cross-linking via fibrinogen or von Willebrand factor binding to the glycoprotein IIb/IIIa receptor. These agents were first evaluated before contemporary antiplatelet and interventional strategies were introduced and in an era when the time to coronary revascularization was substantially longer than today. Thus, limited data are available for glycoprotein IIb/IIIa receptors in patients receiving more potent P2Y12 inhibitors and in those receiving earlier PCI with contemporary drug-eluting stents that have a lower risk for stent thrombosis than prior generations of stents. In current practice, the role of glycoprotein IIb/IIIa receptor inhibitors is largely limited to adjunctive use at the time of PCI in patients with large thrombus burden or as "rescue" or "bailout" therapy in patients with PCI complications such as no-reflow or persistent or recurring thrombus at the lesion.[1]

Recommendation-Specific Supportive Text

1. In a study of 452 selected high-risk patients with large anterior STEMI and a large thrombus burden, adjunctive use of intracoronary abciximab reduced thrombus burden and infarct size.[1] Other trials have also suggested that glycoprotein IIb/IIIa inhibitors can reduce intracoronary thrombus burden in patients with STEMI and NSTE-ACS.[7,8] Thus, glycoprotein IIb/IIIa receptor inhibitors can be considered at the time of PCI for patients with a large coronary thrombus burden or no-reflow or slow flow that is believed to be attributable to distal embolization of thrombus. In clinical trials comparing intravenous and intracoronary administration of glycoprotein IIb/IIIa inhibitors, clinical and bleeding outcomes, as well as thrombus resolution and infarct size, have generally been similar.[2,9,10]
2. Multiple strategies have been evaluated for use of glycoprotein IIb/IIIa receptor inhibitors in patients with ACS. "Upstream" administration of these agents is defined as administration of small molecule agents (eptifibatide or tirofiban) early after

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ACS diagnosis for medical stabilization prior to planned angiography and PCI. In the EARLY-ACS (Early Glycoprotein IIb/IIIa Inhibition in Patients with Non–ST-segment Elevation Acute Coronary Syndrome) trial, 9406 patients with NSTE-ACS were randomized to routine upstream use of eptifibatide (within 8 hours after presentation to the hospital) versus ad hoc adjunctive use at the time of PCI among patients with NSTE-ACS.[4] Ischemic outcomes were not improved and bleeding was increased in the routine upstream eptifibatide arm. An alternative approach is routine adjunctive use of a glycoprotein IIb/IIIa inhibitor at the time of PCI for patients with STEMI or NSTE-ACS. Although early trials performed prior to use of potent P2Y12 inhibitors suggested that this approach improved procedural outcomes and reduced periprocedural myocardial necrosis, studies performed among patients receiving pretreatment with clopidogrel have not confirmed reduction of ischemic events with routine adjunctive glycoprotein IIb/IIIa inhibition and have increased bleeding complications.[5,11]

4.4. Parenteral Anticoagulation

Recommendations for Parenteral Anticoagulation
Referenced studies that support recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
NSTE-ACS: Upstream* Anticoagulant Therapy		
1	B-R	1. In patients with NSTE-ACS, intravenous unfractionated heparin (UFH) is useful to reduce ischemic events.†[1–4]
1	B-R	2. In patients with NSTE-ACS in whom an early invasive approach is not anticipated, either enoxaparin or fondaparinux are recommended alternatives to UFH to reduce ischemic events.[5–11]
Anticoagulant Therapy in Patients Undergoing Coronary Revascularization		
1	C-LD	3. In patients with ACS undergoing coronary revascularization (CABG or PCI) in the same admission, parenteral anticoagulation should be continued until revascularization to reduce ischemic events.[12,13]
Anticoagulant Therapy to Support PCI in ACS (STEMI and NSTE-ACS)		
1	C-EO	4. In patients with ACS undergoing PCI, intravenous UFH is useful to reduce ischemic events.†
1	B-R	5. In patients with STEMI undergoing PCI, bivalirudin is useful as an alternative to UFH to reduce mortality and bleeding.†[14–19]
2b	B-R	6. In patients with NSTE-ACS undergoing PCI, bivalirudin may be reasonable as an alternative to UFH to reduce bleeding.†[16,20–23]
2b	B-R	7. In patients with ACS, intravenous enoxaparin may be considered as an alternative to UFH at the time of PCI to reduce ischemic events.‡[7,8,24–26]
3: Harm	B-R	8. In patients with ACS, fondaparinux should not be used to support PCI because of the risk of catheter thrombosis.[5,27]
STEMI: Anticoagulant Therapy Treated With Fibrinolytic Therapy		
1	A	9. In patients with STEMI treated with fibrinolytic therapy, parenteral anticoagulation should be continued for the duration of the hospital stay (maximum of 8 days) or until revascularization is performed to reduce ischemic events.[9,10,27–29]
1	A	10. In patients with STEMI treated with fibrinolytic therapy who are not intended to undergo an invasive approach, enoxaparin is the recommended anticoagulant to reduce ischemic events.[9,10,28,29]
1	B-R	11. In patients with STEMI treated with fibrinolytic therapy who are not intended to undergo an invasive approach, fondaparinux is a recommended alternative to reduce ischemic events.[27,30]

*At the time of diagnosis and prior to invasive coronary angiography if planned.
†Adapted or
‡modified from the "2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization."[31]

Synopsis

Parenteral anticoagulation is recommended for all patients with ACS, irrespective of the initial treatment strategy, to treat the underlying pathophysiologic process (coronary atherothrombosis) and reduce the risk of recurrent MACE (Table 10). Although eventual diagnostic reclassification can occur (ie, to other nonatherothrombotic ACS diagnoses such as coronary spasm or other conditions that can mimic ACS, such as stress cardiomyopathy or myocarditis), initial parenteral anticoagulation is intended to treat thrombus caused by atherosclerotic plaque disruption (rupture or erosion) in patients with presumed type 1 MI.[32] Anticoagulation strategies are to be initiated upstream (at the time of diagnosis and prior to coronary angiography) and to support PCI or other reperfusion therapy. In patients with ACS undergoing PCI, intraprocedural thrombin generation and platelet aggregation may occur, for which reason parenteral anticoagulation is recommended to reduce the risk for thrombotic complications.[33] The choice of a parenteral anticoagulant can be complex because it is influenced by various factors, including vascular access site, renal function, and concomitant use of other antiplatelet or anticoagulant agents. Heparin-induced thrombocytopenia can occur with both UFH and low-molecular-weight heparin; in this context, argatroban and bivalirudin are direct thrombin inhibitors that are acceptable alternative anticoagulants for patients with known heparin-induced thrombocytopenia.[34,35]

Recommendation-Specific Supportive Text

1. UFH has traditionally been the preferred anticoagulant to treat patients with NSTE-ACS.[1–4] However, limitations to its use include the lack of

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Table 10. Dosing of Parenteral Anticoagulation in ACS

Drug	Dosing
UFH	**Initial therapy:** Loading dose 60 IU/kg (max 4000 IU), with initial infusion 12 IU/kg per h (max 1000 IU/h) adjusted to therapeutic aPTT range of 60-80 s. **To support PCI:** In patients who have received prior anticoagulant therapy, additional UFH as needed to achieve an ACT 250-300 s. In patients who have not received prior anticoagulant therapy, 70-100 U/kg initial bolus to achieve target ACT of 250-300 s. **With fibrinolytic therapy:** Loading dose 60 IU/kg (maximum 4000 IU) with initial infusion 12 IU/kg per h (maximum 1000 IU/h) adjusted to therapeutic aPTT range.
Bivalirudin	**To support PCI:** 0.75 mg/kg bolus, 1.75 mg/kg per h IV infusion during the PCI procedure. **Post-PCI infusion for PPCI:** 1.75 mg/kg per h for 2-4 h post-PCI. In patients with CrCl <30 mL/min, reduced infusion to 1 mg/kg per h.
Enoxaparin	**Initial therapy:** 1 mg/kg subcutaneous every 12 h. Reduce dose to 1 mg/kg per d subcutaneous if CrCl <30 mL/min. **To support PCI:** For previous treatment with enoxaparin, if the last subcutaneous dose was administered 8-12 h earlier or if only 1 subcutaneous dose of enoxaparin has been administered, an IV dose of 0.3 mg of enoxaparin should be given. If the last dose was administered within the previous 8 h, no additional enoxaparin should be given. For patients who have not received prior anticoagulant therapy, 0.5-0.75 mg/kg IV bolus. **With fibrinolytic therapy:** If age <75 y, 30 mg IV bolus, followed in 15 min by 1 mg/kg subcutaneous every 12 h (maximum 100 mg for the first 2 doses). If age ≥75 y: no bolus, 0.75 mg/kg subcutaneous every 12 h (maximum 75 mg for the first 2 doses). Regardless of age, if CrCl <30 mL/min: 1 mg/kg subcutaneous every 24 h.
Fondaparinux	**Initial therapy:** 2.5 mg subcutaneous daily. **With fibrinolytic therapy:** 2.5 mg IV, then 2.5 mg subcutaneous daily starting the following day. Contraindicated if CrCl <30 mL/min. Fondaparinux should not be used to support PCI because of the risk of catheter thrombosis.

ACS indicates acute coronary syndromes; ACT, activated clotting time; aPTT, activated partial thromboplastin time; CrCl, creatinine clearance; PCI, percutaneous coronary intervention; PPCI, primary percutaneous coronary intervention; and UFH, unfractionated heparin.

a predictable dose response and risk of heparin-induced thrombocytopenia.[33] In unstable angina, a meta-analysis including 1353 patients enrolled from 6 randomized studies showed that, in comparison to patients treated with aspirin alone, those treated with aspirin and heparin were at lower, albeit nonstatistically significant, risk for MI or death during the randomized treatment period (relative risk, 0.67 [95% CI, 0.44-1.02]).[3] Its efficacy compared with placebo has not been evaluated in the current era of dual antiplatelet therapy (DAPT) and early revascularization.[33]

2. Fondaparinux, a synthetic pentasaccharide that selectively binds antithrombin and causes rapid and predictable inhibition of Factor Xa, was evaluated in patients with high-risk NSTE-ACS in the OASIS-5 (Fifth Organization to Assess Strategies in Acute Ischemic Syndromes) trial.[5] Fondaparinux was similar to enoxaparin in the risk for ischemic events at 9 days, but it reduced major bleeding. About 40% of the patients underwent PCI, and an increase was observed in the rate of guiding-catheter thrombus formation with fondaparinux (0.9% versus 0.3%) compared with enoxaparin. In NSTE-ACS, despite some data favoring the use of enoxaparin over UFH,[11] multiple meta-analyses have not demonstrated compelling superiority in efficacy over UFH.[7,26,36] A meta-analysis comparing low-molecular-weight heparin to UFH in 12 171 patients with ACS without ST-segment elevation across 5 randomized trials showed no significant difference in death or MI (2.2% versus 2.3%) or in the risk of major bleeding.[36]
3. For patients with ACS undergoing coronary revascularization (CABG or PCI), parenteral anticoagulation is indicated until revascularization. The premature discontinuation of anticoagulation is associated with a transient rebound increase in thrombin activity and activated protein C and the reactivation of ischemic events,[12,13] with the greatest risk for reinfarction in the first 4 to 8 hours after the discontinuation of anticoagulation.
4. UFH has traditionally been the preferred anticoagulant to support PCI in patients with NSTE-ACS. Activated clotting time is used to guide dosing during PCI.[37] Although its pharmacokinetic effects are not always predictable, its anticoagulant effect is reversible with the administration of protamine.
5. Bivalirudin is a direct thrombin inhibitor evaluated in both NSTE-ACS and STEMI that can be used to support PCI. In the BRIGHT-4 (Bivalirudin with Prolonged Full-Dose Infusion during PPCI versus Heparin) trial,[15] which enrolled patients with STEMI undergoing PPCI using radial access (93%), bivalirudin was compared with heparin monotherapy in an open-label design. The bivalirudin regimen used included the standard bolus and dosing (0.75 mg/kg, then 1.75 mg/kg per hour) plus a post-PCI infusion at the full dose (1.75 mg/kg per hour) for 2 to 4 hours. Bivalirudin with the full dose post-PCI infusion was superior to UFH in reducing the 30-day composite of all-cause death or BARC

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(Bleeding Academic Research Consortium) types 3-5 bleeding (4.39% versus 3.06%; *P*=0.007).[15] All-cause death was also reduced with bivalirudin (3.92% versus 2.96%; *P*=0.04), as well as 30-day stent thrombosis (0.37% versus 1.1%; *P*=0.0015). Based on these results, when bivalirudin is used to support PPCI for STEMI, a postprocedure 2- to 4-hour infusion at full dose is recommended.[15,38,39]

6. Meta-analyses comparing bivalirudin versus UFH with or without glycoprotein IIb/IIIa inhibitors in patients with ACS demonstrate that bivalirudin is associated with a lower risk for major bleeding.[16,17,40] In the context of NSTE-ACS, bivalirudin was evaluated in the ACUITY (A Comparison of Angiomax Versus Heparin in Acute Coronary Syndromes) trial, where bivalirudin was noninferior to UFH plus glycoprotein IIb/IIIa inhibitor for the risk of MACE and superior with respect to 30-day major bleeding.[41] The bleeding definition used in the study was specific to the ACUITY trial. Bivalirudin was also evaluated in the MATRIX (Minimizing Adverse Hemorrhagic Events by Transradial Access Site and Systemic Implementation of AngioX) trial where it was compared against UFH alone (ie, without concomitant glycoprotein IIb/IIIa inhibitor).[42] No significant difference was observed between the 2 arms with respect to 30-day ischemic or bleeding events.
7. Intravenous enoxaparin compared with UFH reduces the risk for ischemic outcomes without a significant difference in bleeding in the setting of PPCI. In the ATOLL (Acute Myocardial Infarction Treated with Primary Angioplasty and Intravenous Enoxaparin or Unfractionated Heparin to Lower Ischemic and Bleeding Events at Short- and Long-term Follow-up) trial,[24] which enrolled patients presenting with STEMI, the primary endpoint of 30-day incidence of death, complication of MI, procedural failure, or major bleeding occurred in 28% of patients with enoxaparin compared with 34% with UFH (*P*=0.06). Although the incidence of primary endpoint was not significantly different between enoxaparin and UFH, the secondary endpoint of 30-day death, recurrent ACS, or urgent revascularization was significantly lower in the enoxaparin group (7% versus 11%; *P*=0.015). In addition, a net clinical benefit (death, complication of MI, or major bleeding) was observed with enoxaparin compared with UFH (10% versus 15%; *P*=0.03). In a meta-analysis of 10 451 patients, intravenous enoxaparin was associated with a significant reduction in death and major bleeding.[26]
8. Fondaparinux should not be used as the sole anticoagulant to support PCI because of the risk of catheter thrombosis.[5,27,31] In the OASIS-5 trial, an increase was observed in the rate of catheter-related thrombus with fondaparinux compared with enoxaparin (0.9% versus 0.4%).[5] Similar results were observed in the OASIS-6 (The Safety and Efficacy of Fondaparinux versus Control Therapy in Patients with STEMI) trial in which a higher rate of guiding-catheter thrombosis and more coronary complications with fondaparinux were observed when used during PCI.[27]
9. In patients with STEMI treated with fibrinolytic therapy, parenteral anticoagulation is recommended before and after fibrinolytic therapy to reduce ischemic events. In studies of fibrinolytic therapy such as the GUSTO (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) trial, the ASSENT-3 (Assessment of the Safety and Efficacy of a New Thrombolytic Regimen) trial, or the ExTRACT-TIMI 25 (Enoxaparin and Thrombolysis Reperfusion for Acute Myocardial Infarction Treatment-Thrombolysis in Myocardial Infarction 25) study, intravenous heparin was administered for at least 48 hours.[10,29,43] In the ExTRACT-TIMI 25 study, the UFH infusion was given for at least 48 hours but could be continued for a longer period at the treating physician's discretion, whereas the subcutaneous injections of enoxaparin were continued until hospital discharge or for a maximum of 8 days (whichever came first).[10] Patients randomized to enoxaparin had a lower risk of death or nonfatal recurrent MI through 30 days compared with UFH (9.9% versus 12.0%); however, treatment with enoxaparin was associated with an increase in major bleeding (2.1% versus 1.4%).[10]
10. In patients with STEMI who received fibrinolytic therapy and who are not planned for an invasive approach, enoxaparin is the preferred anticoagulant over UFH.[9,10,28,29,44] In the ExTRACT-TIMI 25 study, enoxaparin until hospital discharge or for a maximum of 8 days (whichever came first) was compared with UFH administered for at least 48 hours (could be continued for a longer period at the treating physician's discretion) in 20 506 patients with STEMI receiving fibrinolytic therapy.[10] The primary endpoint of death or nonfatal recurrent MI through 30 days occurred in 12% in the UFH group compared with 9.9% in the enoxaparin group. In a meta-analysis of 14 randomized trials, UFH did not reduce reinfarction or death in patients treated with fibrinolytic therapy. In contrast, low-molecular-weight heparin reduced the risk of reinfarction and death compared with placebo and the risk of reinfarction.[45]
11. In patients with STEMI who are not likely to undergo an invasive approach, fondaparinux is an alternate anticoagulant that can be used. In the OASIS-6 trial of patients with STEMI who were treated with thrombolytic agents (predominantly streptokinase),

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fondaparinux significantly reduced the risk of the primary endpoint of death or reinfarction at 30 days, including a significant reduction in mortality, reinfarction, and severe bleeding when compared with placebo or UFH.[27,30]

4.5. Lipid Management

Recommendations for Lipid Management
Referenced studies that support recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
1	A	1. In patients with ACS, high-intensity statin therapy is recommended to reduce the risk of MACE.*[1–4]
1	A	2. In patients with ACS who are already on maximally tolerated statin therapy with low-density lipoprotein cholesterol (LDL-C) ≥70 mg/dL (≥1.8 mmol/L), adding a nonstatin lipid-lowering agent is recommended to further reduce the risk of MACE.†[5–7]
1	B-R	3. In patients with ACS who are statin intolerant, nonstatin lipid-lowering therapy is recommended to lower LDL-C and reduce the risk of MACE.[8–10]
2a	B-R	4. In patients with ACS who are already on maximally tolerated statin therapy with LDL-C 55 to 69 mg/dL (≥1.4 to <1.8 mmol/L), adding a nonstatin lipid-lowering agent is reasonable to reduce the risk of MACE.*[5–7,11–13]
2b	B-R	5. In patients with ACS, the concurrent initiation of ezetimibe in combination with maximally tolerated statin may be considered to reduce the risk of MACE.[5]

*Modified or
†adapted from the "2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline for the Management of Patients With Chronic Coronary Disease."[14]

Synopsis

The current recommendations focus on patients with recent (ie, within 12 months) ACS. The 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA CCD guideline provides more detailed recommendations on long-term management of lipids in patients with prior ACS.[14] ASCVD event rates are substantially higher in patients with recent ACS than those with CCD, with 1-year rates of cardiovascular death, MI, and ischemic stroke estimated at 10% to 15% after an ACS hospitalization.[15,16] Higher risk among patients with ACS supports more aggressive LDL-cholesterol (LDL-C) targets in patients with recent ACS compared with those with CCD (Figure 5).[14–16] RCTs have demonstrated ASCVD event reduction with multiple different pharmacological approaches to LDL-C level lowering, with the magnitude of benefit proportional to the degree of LDL-C level lowering.[17] In patients with ACS, RCTs have demonstrated incremental benefit with high- compared with moderate-intensity statin therapy in regard to reduction in MACE.[1–4] For patients who do not reach LDL-C treatment goals on maximally tolerated statin therapy, or who are intolerant to statins, several nonstatin therapies, including ezetimibe, monoclonal antibodies to proprotein convertase subtilisin/kexin type 9 (PCSK9), and bempedoic acid, can both lower LDL-C levels and improve ASCVD outcomes across diverse populations.[5–10] Inclisiran also lowers LDL-C levels by preventing translation of PCSK9 mRNA, but clinical outcomes studies are not yet available (Table 12). Nonetheless, the relative benefit of LDL-C–lowering therapies is expected to be proportional to the observed reduction in LDL-C levels (Tables 11 and 12).[5–11] A lipid profile is recommended as soon as feasible after presentation with ACS (Figure 5), because LDL-C levels decrease modestly beginning 24 hours from symptom onset.[18] Lipid management after hospital discharge is discussed in Section 11.2, "Reassessment of Lipid Levels Postdischarge."

Recommendation-Specific Supportive Text

1. High-intensity statin regimens lower LDL-C concentration by an average of ≥50% (Table 11). The CTT (Cholesterol Treatment Trialists) meta-analysis of 5 RCTs showed that LDL-C concentration lowering with high-intensity statins compared with moderate-intensity statins reduces major vascular events by approximately 15% in patients with coronary artery disease (CAD).[4] An individual participant meta-analysis of the A to Z (Aggrastat to Zocor) and PROVE IT (Pravastatin or Atorvastatin Evaluation and Infection Therapy)-TIMI 22 trials, both of which were performed in patients stabilized early after ACS, demonstrated significant reductions in cardiovascular and all-cause death with more intensive versus less intensive statin regimens.[19] The benefit of a high-intensity statin regimen appears early after ACS and persists over time.[3] The benefit of high-intensity statins after ACS appears to be independent of baseline LDL-C concentration. No indication was observed of any safety concerns from achieving very low LDL-C concentrations on statins or other lipid-lowering therapies; therefore, high-intensity statin therapy should not be de-escalated during follow-up in patients who are tolerating treatment.[13]
2. Multiple therapeutic options are now available to add to maximally tolerated statin therapy to achieve desired LDL-C goals in patients with ACS (Table 12). In IMPROVE IT (Improved Reduction of Outcomes; Vytorin Efficacy International Trial), addition of ezetimibe to simvastatin 40 mg daily in patients <10 days after ACS led to a modest but significant reduction in MACE, over a median follow-up of 6 years.[5] Clinical trials of PCSK9 inhibitors have demonstrated a 15% relative risk reduction in MACE over a median of 2 to 3 years including patients >1 month after ACS.[6,7,20] Greater absolute benefit with PCSK9 inhibitors has been

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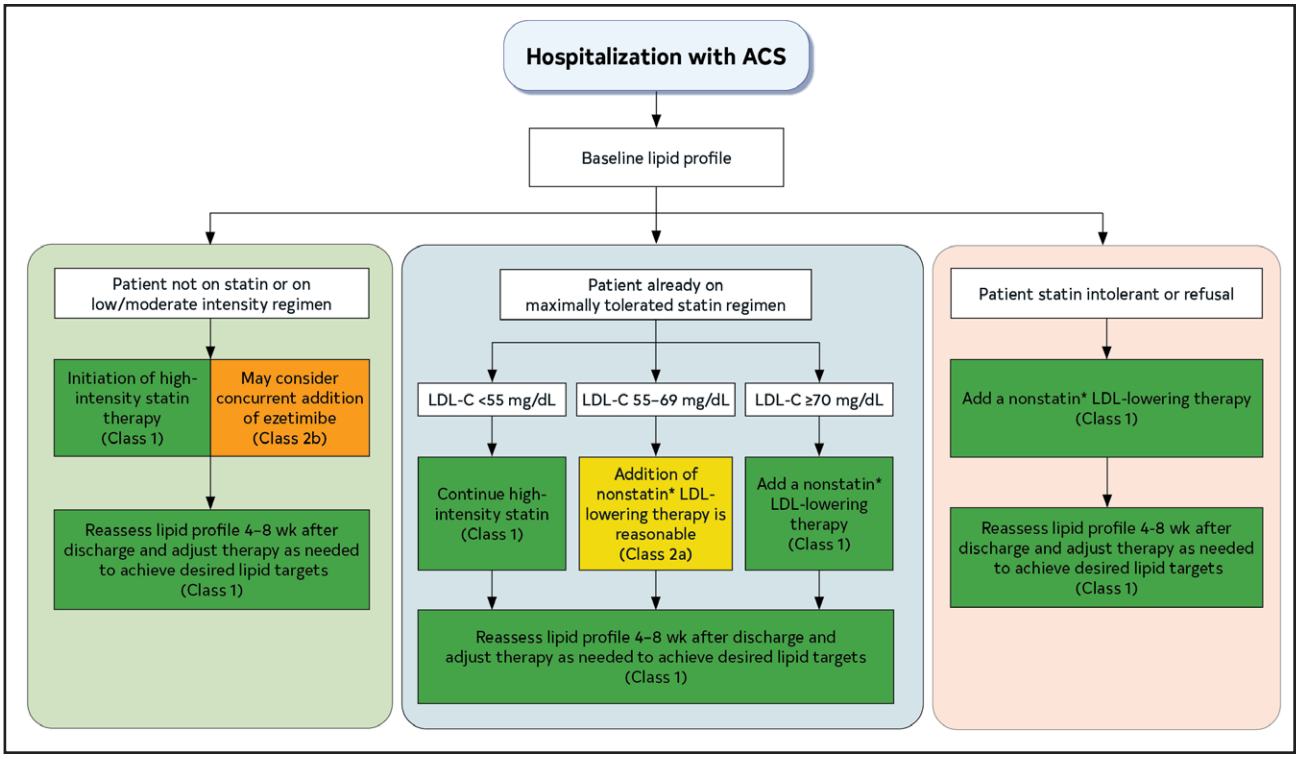
Hospitalization with ACS
Baseline lipid profile
Patient not on statin or on low/moderate intensity regimen
Initiation of high-intensity statin therapy (Class 1)
May consider concurrent addition of ezetimibe (Class 2b)
Reassess lipid profile 4–8 wk after discharge and adjust therapy as needed to achieve desired lipid targets (Class 1)
Patient already on maximally tolerated statin regimen
LDL-C <55 mg/dL
LDL-C 55–69 mg/dL
LDL-C ≥70 mg/dL
Continue high-intensity statin (Class 1)
Addition of nonstatin* LDL-lowering therapy is reasonable (Class 2a)
Add a nonstatin* LDL-lowering therapy (Class 1)
Reassess lipid profile 4–8 wk after discharge and adjust therapy as needed to achieve desired lipid targets (Class 1)
Patient statin intolerant or refusal
Add a nonstatin* LDL-lowering therapy (Class 1)
Reassess lipid profile 4-8 wk after discharge and adjust therapy as needed to achieve desired lipid targets (Class 1)

Figure 5. Management of Lipid-Lowering Therapy for Patients With ACS.
Colors correspond to Class of Recommendation in Table 2.
*Nonstatin LDL-lowering therapy: ezetimibe, PCSK9 inhibitor (alirocumab, evolocumab and inclisiran), and/or bempedoic acid.
ACS indicates acute coronary syndromes; LDL, low-density lipoprotein; LDL-C, low-density lipoprotein cholesterol; and PCSK9, proprotein convertase subtilisin/kexin type 9.

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demonstrated in those patients enrolled closer to their ACS event.[20,21] Evolocumab effectively reduces LDL-C levels early after ACS and has demonstrated favorable changes on plaque components by intracoronary imaging in patients with NSTEMI.[22–24] Greater plaque regression has also been reported by intracoronary imaging for patients treated with alirocumab after AMI.[25] Inclisiran is a small interfering RNA targeting synthesis of the PCSK9 protein that is administered at 6-month intervals after an initial 3-month dose. Inclisiran lowers LDL-C levels by approximately 50% and is well tolerated,[26] but clinical outcome studies are not yet available. Bempedoic acid works upstream from statins in the liver and leads to approximately 20% reduction in LDL-C levels. It reduces MACE

Table 11. Nonstatin Treatment Options for LDL-C Lowering in Patients With ACS Who Are Not at LDL-C Goal on Maximally Tolerated Statin Therapy

Drug	Mechanism of Action	LDL-C Lowering (%)	Outcomes Study Performed in Patients With Recent ACS?	Potential Adverse Effects
Ezetimibe*	Blocks NPC1L1 cholesterol absorption	15-25	Yes (<10 d post ACS)	Hyperuricemia
Evolocumab	Monoclonal antibody to PCSK9	~60	Established ASCVD (>1 mo post ACS)	Injection site reaction
Alirocumab	Monoclonal antibody to PCSK9	~60	Yes (1-12 mo post ACS)	Injection site reaction
Inclisiran	Inhibitor of PCSK9 synthesis (small interfering RNA)	~50	Clinical outcomes trials in ASCVD are ongoing	Injection site reaction
Bempedoic acid†	ATP-citrate lyase inhibitor	~20	With or at high risk for CVD (>90 d post ACS)	Gout; gallstones; liver function test abnormalities

All agents are approved by the FDA.
*The LDL-C lowering potency of ezetimibe is greater when used in combination with statin therapy (approximately 25% LDL-C reduction) than when used as monotherapy (15%-20%).
†Coadministration of bempedoic acid with simvastatin at a dose >20 mg and pravastatin at a dose >40 mg is not recommended due to the increased risk of muscle-related adverse effects from statins.
ACS indicates acute coronary syndromes; ASCVD, atherosclerotic cardiovascular disease; CVD, cardiovascular disease; FDA, US Food and Drug Administration; LDL-C, low-density lipoprotein cholesterol; NPC1L1, Niemann-Pick C1-Like 1 protein; and PCSK9, proprotein convertase subtilisin/kexin type 9.

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Table 12. Statin Classification

Statin Classification by Expected LDL-C Reduction		
High-Intensity Therapy*	Moderate-Intensity Therapy†	Low-Intensity Therapy‡
Atorvastatin 40-80 mg	Atorvastatin 10-20 mg	Simvastatin 10 mg
Rosuvastatin 20-40 mg	Rosuvastatin 5-10 mg	Pravastatin 10-20 mg
	Simvastatin 20-40 mg	Lovastatin 20 mg
	Pravastatin 40-80 mg	Fluvastatin 20-40 mg
	Lovastatin 40 mg	
	Fluvastatin XL 80 mg	
	Fluvastatin 40 mg BID	
	Pitavastatin 1-4 mg	

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*Expected LDL-C reduction ≥50%.

†Expected LDL-C reduction ≥30% to 49%.

‡Expected LDL-C reduction <30%.

BID indicates twice daily; LDL-C, low-density lipoprotein cholesterol.

by 13% in statin-intolerant patients when started >90 days after ACS.[10]

3. Statin intolerance is frequent in clinical practice and the most commonly reported cause is statin-associated muscle symptoms.[27] To consider a patient as having statin intolerance, a minimum of 2 statins should be attempted, including at least 1 at the lowest approved daily dose.[28] Currently available options for patients with complete or partial intolerance to statin therapy include ezetimibe, PCSK9 inhibitor monoclonal antibodies, inclisiran, and bempedoic acid. Ezetimibe and PCSK9 inhibitors have been demonstrated to be safe and well tolerated and improve lipid parameters in statin-intolerant patients.[8,9] However, outcomes studies using these agents as monotherapy or in combination in statin-intolerant patients are not available. Bempedoic acid is an ATP citrate lyase inhibitor that reduces LDL-C levels by 15% to 25% with low rates of muscle-related adverse effects.[29,30] A combination product that combines bempedoic acid with ezetimibe lowered LDL-C levels by approximately 35%.[31] In the CLEAR Outcomes (Cholesterol Lowering via Bempedoic Acid, an ACL-Inhibiting Regimen) trial, bempedoic acid was compared with placebo in statin-intolerant patients with or at high risk for ASCVD. Patients with ACS within 90 days prior to randomization were excluded from this trial. Mean LDL-C level was 139 mg/dL at enrollment and was reduced by 29 mg/dL with bempedoic acid compared with placebo. MACE was reduced by 13% in the bempedoic acid arm. Bempedoic acid raised uric acid levels in a small subset of patients, and rates of abnormal liver function tests, gout, and gallstones were increased with its use in the trial.[10]
4. IMPROVE IT randomized patients post-ACS with LDL-C levels of ≥50 mg/dL and ≤125 mg/dL (≤100 mg/dL if on lipid-lowering therapy) to the combination of simvastatin (40 mg) and ezetimibe (10 mg) or simvastatin (40 mg) and placebo (simvastatin monotherapy), with median LDL-C level at enrollment of 69.5 mg/dL. The addition of ezetimibe reduced the relative risk of MACE by 6.4% compared with placebo.[5] Benefit was similar among patients with baseline LDL-C 50 to 70 mg/dL versus ≥70 mg/dL.[32] FOURIER (Further Cardiovascular Outcomes Research With PCSK9 Inhibition in Subjects With Elevated Risk) and ODYSSEY OUTCOMES (Evaluation of Cardiovascular Outcomes After an Acute Coronary Syndrome During Treatment With Alirocumab) enrolled patients with LDL-C ≥70 mg/dL and thus did not specifically assess outcomes associated with adding PCSK9 inhibitor therapy among patients with LDL-C levels 55 to 70 mg/dL.[6,7] However, secondary analyses of both trials demonstrated better outcomes in patients with achieved LDL-C <50 mg/dL versus those with achieved LDL-C levels ≥50 mg/dL, with monotonic relationships, suggesting better outcomes with progressively lower LDL-C even well below 50 mg/dL.[11,12] Rates of neurocognitive and muscle events, including hemorrhagic stroke, were not increased among patients who achieved very low LDL-C levels with PCSK9 inhibition.[11,12] Longer term follow-up studies support continued benefit and safety associated with achieving and maintaining very low LDL-C levels in secondary prevention with a PCSK9 inhibitor over several years.[33] The benefits of ezetimibe and PCSK9 inhibitors appear to be greater among higher risk patients with prior ACS and diabetes or more advanced coronary or polyvascular disease or elevated biomarkers.[20,34–41]
5. Ezetimibe reduces LDL-C levels by 15% to 25% by blocking its absorption from the gastrointestinal tract via the Niemann-Pick C1-Like 1 protein (NPC1L1). The IMPROVE IT trial studied the combination of simvastatin (40 mg) and ezetimibe (10 mg) (simvastatin-ezetimibe) to simvastatin (40 mg) and placebo (simvastatin monotherapy) in patients hospitalized with an ACS in the past 10 days. The median time from ACS to randomization was 5 days, and 34% of patients were already on a statin at the time of the ACS event. The addition of ezetimibe reduced the relative risk of MACE by 6.4% compared with placebo (hazard ratio, 0.936 [95% CI, 0.89-0.99]) over a median of 6 years' follow-up. Ezetimibe was well-tolerated without any clear imbalances in adverse events compared with placebo.[5]

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4.6. Beta-Blocker Therapy

Recommendation for Beta-Blocker Therapy Referenced studies that support recommendation are summarized in the Evidence Table.		
COR	**LOE**	**Recommendation**
1	A	**1.** In patients with ACS without contraindications, early (<24 hours) initiation of oral beta-blocker therapy is recommended to reduce risk of reinfarction and ventricular arrhythmias.[1–5]

Synopsis

Beta blockers decrease myocardial oxygen demand by reducing the heart rate, blood pressure, and myocardial contractility.[1,3] The clinical benefit of beta blockers in patients with left ventricular ejection fraction (LVEF) <40% and stabilized HF is well established, including patients post-MI.[3–5] Most of the RCT data pertaining to early use of beta-blocker therapy in STEMI were conducted in the pre-reperfusion era.[3] No adequately powered RCTs have been done that examine the clinical benefit of beta blockers during hospitalization among patients exclusively with NSTE-ACS. Although most studies were conducted in patients with STEMI, early hospital initiation of beta-blocker therapy (within 24 hours) is recommended among most patients with ACS and without contraindications (eg, acute HF [Killip class II-IV], evidence of low cardiac output state or at risk for cardiogenic shock, PR interval >0.24 milliseconds, second- or third-degree heart block without a cardiac pacemaker, severe bradycardia, active bronchospasm).[1,2,6] Patients with an initial contraindication to beta-blocker therapy on presentation can be reassessed after 24 hours and initiated on oral beta-blocker therapy if the initial contraindication has resolved. Further study is warranted to examine the benefit in those patients with NSTE-ACS. Although an open-label randomized trial has raised questions about the benefit of long-term beta-blocker therapy following hospital discharge in patients with ACS who have undergone coronary revascularization and have preserved left ventricular (LV) function,[7] this area remains under study.

Recommendation-Specific Supportive Text

1. RCTs from both the pre-reperfusion era and in the early reperfusion era have shown that early initiation of beta-blocker therapy reduces the risk of reinfarction and ventricular arrhythmias among patients with STEMI.[1–3] The COMMIT (Clopidogrel and Metoprolol in Myocardial Infarction) trial included 45 852 patients (approximately 50% received fibrinolytic therapy and 7% having NSTE-ACS) and showed that early initiation of high doses (ie, up to 15 mg intravenously then 200 mg orally daily) of metoprolol reduced the risk of reinfarction and ventricular fibrillation compared with placebo but increased the risk of cardiogenic shock that occurred mainly during the first 24 hours.[1] In a small open-label trial of 801 patients with STEMI who underwent PPCI, carvedilol did not reduce MACE over 3 years, but the trial was underpowered to detect a difference.[8] Overall, the weight of the evidence suggests that a low dose of oral beta blocker should be initiated in patients without contraindication early after diagnosis of ACS (<24 hours) with slow dose escalation as blood pressure and heart rate permit. Use should be discontinued in those with new or worsening HF symptoms or signs of cardiogenic shock. In hemodynamically stable patients with STEMI who do not have acute HF, intravenous beta blockers can be administered prior to reperfusion if there are ongoing symptoms or a clinical indication for administration. The weight of the evidence does not support the routine use of intravenous beta blockers prior to PPCI because of inconsistent results as to whether it has any favorable effect on infarct size or clinical outcomes.[9,10] The optimal duration of beta-blocker use remains unclear in patients with preserved LVEF. Although a randomized trial did not confirm long-term benefit from continued use of a beta blocker after hospital discharge in lower risk patients with preserved LV function who had undergone coronary revascularization,[7] additional studies are ongoing in this space.

4.7. Renin-Angiotensin-Aldosterone System Inhibitors

Recommendations for Renin-Angiotensin-Aldosterone System Inhibitors Referenced studies that support recommendations are summarized in the Evidence Table.		
COR	**LOE**	**Recommendations**
1	A	1. In high-risk patients with ACS (LVEF ≤40%, hypertension, diabetes mellitus, or STEMI with anterior location), an oral angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin receptor blocker (ARB) is indicated to reduce all-cause death and MACE.[1–6]
1	B-R	2. In patients with ACS and LVEF ≤40%, and with HF symptoms and/or diabetes mellitus, a mineralocorticoid receptor antagonist is indicated to reduce all-cause death and MACE.[7]
2a	A	3. In patients with ACS who are not considered high risk, an oral ACEi or an ARB is reasonable to reduce MACE.[4]

Synopsis

Oral ACE inhibitors reduce all-cause death and MACE in patients with STEMI or NSTEMI, particularly when associated with high-risk features (LVEF ≤40%, hypertension, diabetes mellitus, or STEMI with anterior location).[1–4,6] Even in AMI without high-risk features, use of an oral ACEi

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confers a modest survival benefit.[4] Compared with ACEi, the benefits of an ARB in patients with AMI with HF or LV systolic dysfunction are similar.[5] Thus, in the absence of contraindications, either an oral ACEi or ARB should be initiated in appropriate patients with AMI.[5,8] In patients with AMI with LVEF ≤40%, and with HF symptoms and/or diabetes mellitus, the addition of a mineralocorticoid receptor antagonist reduced all-cause death and MACE and should be given in the absence of advanced chronic kidney disease, hyperkalemia, or other contraindication.

In patients with symptomatic HF and reduced LVEF, sacubitril-valsartan has been demonstrated to be superior to an ACEi for reducing cardiovascular death or HF hospitalization; however, the trial excluded patients within 3 months of ACS.[9] In a trial of patients early after MI with LVEF ≤40% and/or pulmonary congestion, sacubitril-valsartan did not significantly reduce cardiovascular death or incident HF compared with an ACEi. Hypotensive events were more common with sacubitril-valsartan, but no other safety concerns were observed. Therefore, if treatment with sacubitril-valsartan for HF with reduced ejection fraction is planned, initiation of this combination agent instead of an ACEi or ARB early after MI appears safe.[10]

Recommendation-Specific Supportive Text

1. Randomized controlled trials have demonstrated a reduction in all-cause death and MACE with the addition of an oral ACEi in patients with AMI with LVEF ≤40%[1,3] and in patients with anterior STEMI.[2] An individual-patient meta-analysis of 98 496 patients with AMI also showed a survival benefit with ACEi use, with the greatest absolute benefit in patients with hypertension, diabetes, and STEMI of anterior location.[4] In the VALIANT (Valsartan in Acute Myocardial Infarction) trial of patients with AMI with LV systolic dysfunction and/or HF symptoms, the use of an ARB was statistically noninferior to an ACEi, and rates of all-cause death were similar between the 2 treatment arms.[5] Concomitant initiation of both an ACEi and ARB in patients with AMI should be avoided due to an increase in adverse events without added benefit compared with either drug alone.[5,8]
2. In the EPHESUS (Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study) trial, the mineralocorticoid receptor antagonist eplerenone reduced both all-cause death and MACE during a mean follow-up of 16 months in patients with AMI with LVEF ≤40% who also had symptoms of HF and/or diabetes mellitus. The use of evidence-based therapies for this population was relatively high, including 86% use of ACEi or ARB and 75% use of a beta blocker at enrollment.[7] Patients with advanced chronic kidney disease (serum creatinine >2.5 mg/dL) or hyperkalemia (serum potassium >5.0 mmol/L) were excluded from enrollment.[7] In a trial of 1012 patients with acute STEMI and without a history of HF, the use of eplerenone reduced the primary endpoint compared with placebo, but the benefit was largely driven by a reduction in natriuretic peptides.[11]
3. The ACE Inhibitor Myocardial Infarction Collaborative Group meta-analysis of 98 496 patients with AMI reported a 30-day mortality rate of 7.1% in AMI patients treated with an ACEi compared with 7.6% receiving placebo (proportional reduction, 7% [95% CI, 2-11]; *P*=0.004), and the benefit appeared to be irrespective of baseline risk.[4] The use of an ACEi also reduced nonfatal cardiac failure compared with placebo.[4]

5. STEMI MANAGEMENT: REPERFUSION STRATEGIES

5.1. Regional Systems of STEMI Care

Recommendation for Regional Systems of STEMI Care
Referenced studies that support recommendation are summarized in the Evidence Table.

COR	LOE	Recommendation
1	B-NR	1. All communities should create and maintain regional systems of STEMI care that coordinate prehospital and hospital-based STEMI care processes with the goal of reducing total ischemic time and improving survival in patients with STEMI.[1–6]

Synopsis

The goal of optimizing outcomes after STEMI depends not only on the efficient execution of STEMI care processes but also on the seamless communication and coordination of care among the teams caring for the patient. The goal of each community is therefore to ensure a coordinated response to every patient with STEMI, regardless of physical location at presentation, to help minimize total ischemic time. The creation and maintenance of successful systems of STEMI care require detailed mapping of care for all possible routes by which a patient with STEMI could present for diagnosis and receive definitive reperfusion therapy at both PCI-capable and non–PCI-capable facilities, as well as access to cardiac surgical care and other advanced care modalities (Figure 6). The many stakeholders of regional systems of STEMI care (including hospitals, EMS companies, regional public health departments, and local governments) must ensure that all components of a STEMI system of care function in a coordinated way with no gaps in care processes to help optimize STEMI outcomes in the community.

Recommendation-Specific Supportive Text

1. The establishment of coordinated regional systems of STEMI care is associated with reduced time to

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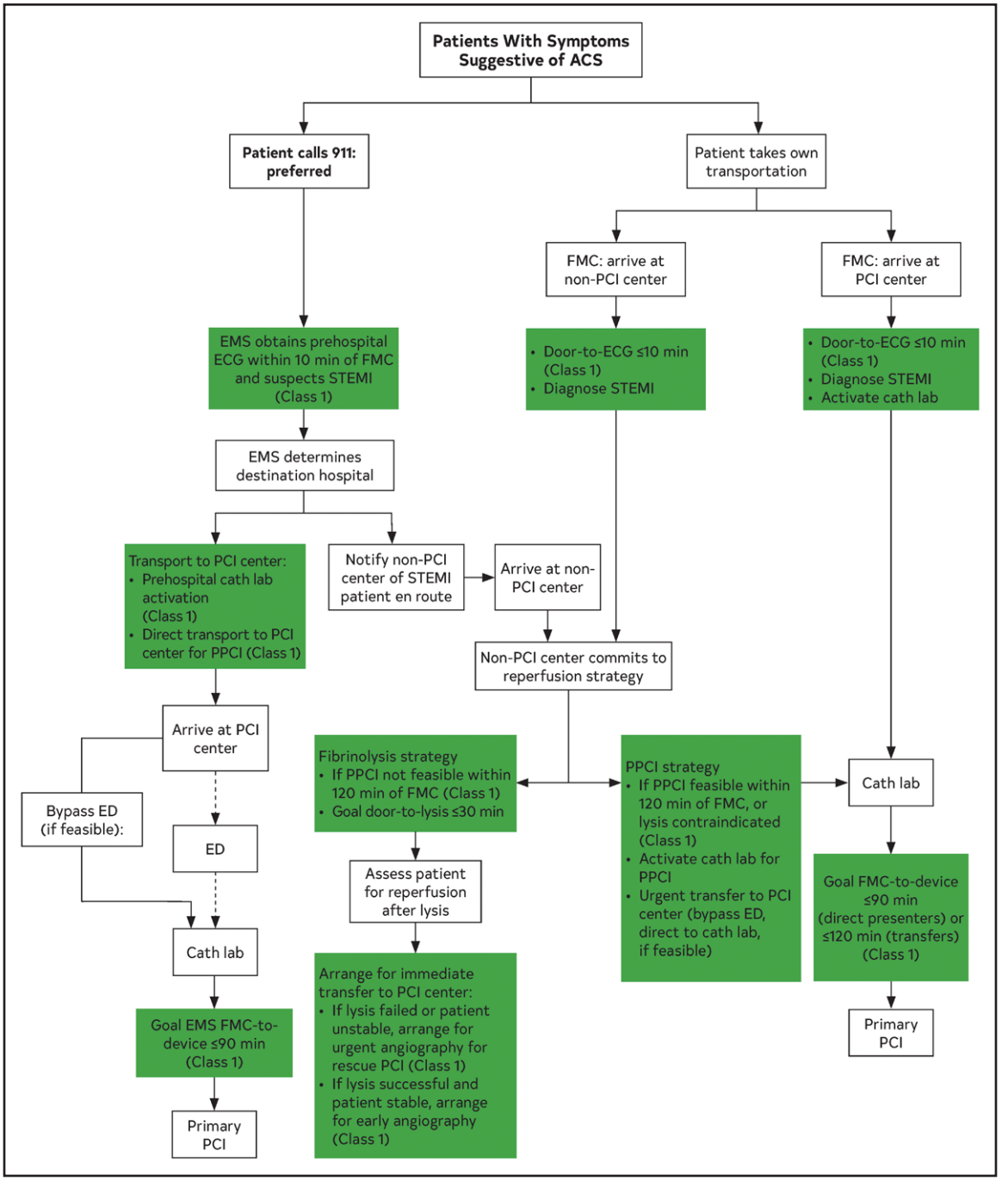
Patients With Symptoms Suggestive of ACS
Patient calls 911: preferred
Patient takes own transportation
FMC: arrive at non-PCI center
FMC: arrive at PCI center
EMS obtains prehospital ECG within 10 min of FMC and suspects STEMI (Class 1)
• Door-to-ECG ≤10 min (Class 1)
• Diagnose STEMI
• Door-to-ECG ≤10 min (Class 1)
• Diagnose STEMI
• Activate cath lab
EMS determines destination hospital
Transport to PCI center:
• Prehospital cath lab activation (Class 1)
• Direct transport to PCI center for PPCI (Class 1)
Notify non-PCI center of STEMI patient en route
Arrive at non-PCI center
Non-PCI center commits to reperfusion strategy
Arrive at PCI center
Bypass ED (if feasible):
ED
Cath lab
Goal EMS FMC-to-device ≤90 min (Class 1)
Primary PCI
Fibrinolysis strategy
• If PPCI not feasible within 120 min of FMC (Class 1)
• Goal door-to-lysis ≤30 min
Assess patient for reperfusion after lysis
Arrange for immediate transfer to PCI center:
• If lysis failed or patient unstable, arrange for urgent angiography for rescue PCI (Class 1)
• If lysis successful and patient stable, arrange for early angiography (Class 1)
PPCI strategy
• If PPCI feasible within 120 min of FMC, or lysis contraindicated (Class 1)
• Activate cath lab for PPCI
• Urgent transfer to PCI center (bypass ED, direct to cath lab, if feasible)
Cath lab
Goal FMC-to-device ≤90 min (direct presenters) or ≤120 min (transfers) (Class 1)
Primary PCI

Figure 6. Care System Pathway for Patients Experiencing Ischemic Symptoms Suggestive of ACS.
Systems of STEMI care, and the most common routes by which patients present for diagnosis and definitive reperfusion therapy for STEMI. Best clinical practice consists of patients calling 9-1-1 (or other emergency services) to activate EMS; EMS obtaining a prehospital ECG, activating the cardiac catheterization laboratory from the field for suspected STEMIs, and transporting the patient to the nearest PCI center when possible; and achieving a system goal of FMC-to-device time within 90 minutes. Colors correspond to Class of Recommendation in Table 2. *Patients with chest tightness or other symptoms indicative of a heart attack. ACS indicates acute coronary syndromes; ED, emergency department; EMS, emergency medical services; FMC, first medical contact; PCI, percutaneous coronary intervention; PPCI, primary percutaneous coronary intervention; and STEMI, ST-segment elevation myocardial infarction.

reperfusion and increased survival in STEMI in several pre- versus postimplementation comparison studies throughout the world.[1–6] Over the past 15 years, considerable gains have been made in reducing FMC to reperfusion times in patients with STEMI and these improvements in reperfusion times have been associated with improved outcomes.[5,7] Unfortunately, recent declines have been reported in the rates of achieving established STEMI performance measures,[8] in part due to the COVID-19 pandemic and

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related challenges in ensuring adequate resourcing and staffing of EMS agencies and hospitals. Therefore, all communities should continue to establish, reinvigorate, and maintain regional systems of STEMI care to improve outcomes of patients with STEMI globally. The collection of high-quality data at every stage of care is an inseparable component of a STEMI system of care. Successful STEMI systems have robust mechanisms for (1) educating the public of the need to immediately call 9-1-1 (or other appropriate local emergency services) for ischemic symptoms and not driving themselves to the nearest hospital; (2) data collection that balances the need for adequate data capture without introducing data overburden; (3) data sharing within hospital departments (eg, ED and cardiology) or between hospitals and EMS agencies; and (4) meetings to review and discuss shared data at local and system levels to drive process improvement.

5.2. Reperfusion at PCI-Capable Hospitals

5.2.1. PPCI in STEMI

Recommendations for PPCI in STEMI
Referenced studies that support recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
1	A	1. In patients with STEMI presenting <12 hours after symptom onset, PPCI should be performed with a goal of FMC to device activation of ≤90 minutes, or ≤120 minutes in patients requiring hospital transfer, to improve survival.[1–7]
1	B-R	2. In patients with ACS and cardiogenic shock or hemodynamic instability, emergency revascularization of the culprit vessel by PCI or CABG is indicated to improve survival, irrespective of time from symptom onset.[8–11]
2a	B-NR	3. In patients with STEMI presenting 12 to 24 hours after symptom onset, PPCI is reasonable to improve clinical outcomes.*[12–15]
2a	C-LD	4. In patients with STEMI presenting >24 hours after symptom onset with the presence of ongoing ischemia or life-threatening arrhythmia, PPCI is reasonable to improve clinical outcomes.†[12,14]
3: No Benefit	B-R	5. In patients who are stable with STEMI who have a totally occluded infarct-related artery >24 hours after symptom onset and are without evidence of ongoing ischemia, acute severe HF, or life-threatening arrhythmia, PPCI should not be performed due to lack of benefit.†[16,17]

*Reproduced or
†modified from the "2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization."[18]

Synopsis

Timely PPCI confers improved survival compared with fibrinolytic therapy as primary reperfusion therapy for patients with STEMI.[6,7] Systems of care designed to reduce the time to PPCI for patients with STEMI have been consequential in reducing risk of early death.[19,20] The goal is to provide PPCI as soon as possible after the diagnosis of STEMI is made with first device activation within 90 minutes from FMC among walk-in and EMS-transported patients and 120 minutes for transfer patients from non–PCI-capable facilities.[1–7] The benefit of PPCI begins to diminish for those >12 hours from symptom onset, but there appears to be continued benefit for PPCI through approximately 24 hours.[12,13] In stable asymptomatic patients with an occluded artery >48 hours after symptom onset, routine PCI has not been shown to be beneficial in the absence of ongoing ischemia; the relative utility of routine PCI for asymptomatic patients with STEMI between 24 to 48 hours from symptom onset is less rigorously tested.[14,15] However, coronary revascularization should be considered for patients with late presentations with continued signs and symptoms of ischemia, including cardiogenic shock, acute severe HF, persistent angina, and life-threatening arrhythmias.

Recommendation-Specific Supportive Text

1. PPCI is the recommended reperfusion therapy in patients with STEMI and ischemic symptoms when performed ≤90 minutes (FMC–to–first-device activation) or ≤120 minutes in transfer patients to improve survival.[1–7] The success of PPCI in achieving these goals was facilitated by the introduction in 2006 of the AHA's Mission: Lifeline programs involving EMS and clinicians (eg, emergency medicine, cardiology, nursing) with practiced drill-down programs and regionalization of care[21] that have improved myocardial salvage, as well as reduced risk of death and adverse outcomes.[4,22,23] PPCI is superior to fibrinolytic therapy, which is used when the patient is in a non–PCI-capable hospital and transfer time to a PCI-capable hospital is anticipated to be >120 minutes. Compared with fibrinolytic therapy with a similar treatment delay, PPCI offers higher rates of infarct-related artery patency, and restoring TIMI 3 epicardial flow grade, as well as lower rates of recurrent ischemia, reinfarction, emergency repeat revascularization procedures, intracranial hemorrhage, and death.[6,7] Radial access for PPCI has further reduced death, decreased access site bleeding, decreased the need for transfusion, and reduced acute kidney injury when compared with femoral access (Section 7.1, "Vascular Access Approach for PCI").[24,25]
2. In the SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) trial,[9] reported in 1999, patients with AMI and cardiogenic shock were randomized to medical therapy or emergency revascularization. Among the patients randomized to revascularization, 64% of patients were referred for PCI and 36% for CABG surgery. The median time from randomization to revascularization was 0.9 hours for PCI and 2.7 hours for CABG surgery. Despite lack of a significant difference in

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the primary endpoint of mortality at 30 days, emergency revascularization with either PCI or CABG surgery reduced mortality at 6 months,[9] and the mortality rate benefit was maintained through 1 and 6 years.[26,27] In an observational analysis from the FITT-STEMI (Feedback Intervention and Treatment Times in ST-Elevation Myocardial Infarction) trial, for every 10-minute delay in PPCI after 60 minutes from FMC, there were an additional 3 to 4 deaths per 100 with >80% mortality beyond 6 hours of delay from FMC for patients with cardiogenic shock.[8] Therefore, it is recommended that PPCI should be performed in patients with STEMI and cardiogenic shock as soon as possible, ideally within 90 minutes, to reduce the mortality rate. Observational studies suggest that emergency CABG surgery remains a treatment option in patients with cardiogenic shock who are not amenable to primary reperfusion with PCI[10,11] or when PCI is not successful.[11,28]

3. The benefit of PCI for asymptomatic patients presenting 12 to 24 hours after symptom onset is not well studied. Small randomized trials of patients 12 to 48 hours after symptom onset in STEMI have demonstrated that PPCI reduces infarct size and improves the LVEF.[12,14] These findings are further supported by observational data.[13,15]
4. No dedicated trials have been done that examine the benefit of PPCI in patients with STEMI presenting late >24 hours after symptom onset who have clinical evidence of ongoing ischemia, acute severe HF, or life-threatening arrhythmias. Observational data and small trials suggest that PCI in patients with STEMI with delayed presentations is reasonable and is associated with improved outcomes.[12,14,15]
5. PCI is not recommended for an occluded infarct-related artery if the patient is asymptomatic and has a completed infarct. MACE outcomes were similar in those with an occluded infarct-related artery versus those who underwent PCI 3 to 28 days after an MI (Occluded Artery Trial [OAT])[16] and results were no different at 7 years follow-up.[29] Similar findings were noted in the DECOPI (Desobstruction Coronaire en Post-Infarctus) trial, which enrolled patients with an occluded artery and Q waves on the ECG presenting 2 to 15 days after symptom onset.[17]

5.2.2. Urgent CABG Surgery

Recommendation for Urgent CABG Surgery Referenced studies that support recommendation are summarized in the Evidence Table.		
COR	**LOE**	**Recommendation**
2a	**B-NR**	1. In patients with STEMI in whom PCI is not feasible or successful, with a large area of myocardium at risk, emergency or urgent CABG surgery can be effective to improve clinical outcomes.*[1,2]

*Modified from the "2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization."[3]

Synopsis

Trials that evaluated the efficacy and safety of CABG surgery in STEMI are limited.[4] When PCI is not possible for anatomic reasons or in the presence of complex disease, CABG surgery can be performed as the primary reperfusion strategy. After successful reperfusion of the infarct-related artery, CABG surgery can also be important when managing patients with more extensive noninfarct-related artery disease (Section 7.4.1, "Management of Multivessel CAD in STEMI"). The appropriate timing of CABG surgery in patients with STEMI should be determined on an individual basis, taking into consideration the hemodynamic stability of the patient, the presence of ongoing ischemia, and extent of myocardium at risk. After failed PPCI, emergency CABG surgery is not recommended in the absence of a large area of myocardium at risk or if surgical targets are poor and if surgery may be associated with an increased risk of death and adverse cardiovascular outcomes compared with nonsurgical management.[5] For recommendations regarding CABG surgery in patients presenting with cardiogenic shock or mechanical complications, please refer to Section 8.1, "Revascularization in ACS With Cardiogenic Shock" and Section 9.1, "Mechanical Complications."

Recommendation-Specific Supportive Text

1. No RCTs have been done that compare PPCI with surgical revascularization in the setting of STEMI. For patients with STEMI who are hemodynamically stable with anatomy of the infarct-related artery that is not amenable to PPCI, or if PPCI is unsuccessful, CABG surgery can be useful if there is a large area of myocardium at risk. In such patients, particularly in the presence of ongoing ischemia or if a large area of myocardium is at risk, CABG surgery may be effectively performed as a primary reperfusion strategy or after PPCI.[1,2] Despite an increase in the acuity of presentation and the burden of comorbidities, the in-hospital mortality rate after CABG surgery in patients with STEMI continues to decrease.[1,4]

5.3. Reperfusion at Non–PCI-Capable Hospitals

Recommendations for Reperfusion at Non–PCI-Capable Hospitals Referenced studies that support recommendations are summarized in the Evidence Table.		
COR	**LOE**	**Recommendations**
1	**A**	1. In patients with STEMI and an estimated time from FMC to device activation of ≤120 minutes or those with a contraindication to fibrinolytic therapy, transfer to a PCI-capable hospital for PPCI is recommended to reduce MACE.[1–3]
1	**A**	2. In patients with STEMI and symptom onset of <12 hours and anticipated delay to PPCI >120 minutes from FMC, fibrinolytic therapy should be administered in patients without contraindication to reduce MACE.[4–10]

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Recommendations for Reperfusion at Non–PCI-Capable Hospitals (Continued)		
COR	LOE	Recommendations
2a	B-NR	3. In patients with STEMI and symptom onset of 12 to 24 hours, transfer to a PCI-capable hospital for PPCI is reasonable to reduce infarct size and MACE.[11,12]
3: Harm	B-R	4. In patients with only ST-segment depression, except when true posterior STEMI is suspected, fibrinolytic therapy should not be administered due to risk of hemorrhagic stroke and major noncerebral bleeding.[13]

Synopsis

A large proportion of patients globally live >1 hour driving time to a PCI-capable hospital.[14–17] At non–PCI-capable hospitals, transfer for PPCI is recommended if device activation can be reasonably predicted to occur in <2 hours from FMC. If this cannot be achieved and symptoms have been present <12 hours, fibrinolytic therapy is recommended to reduce the risk of recurrent MACE. Patients with STEMI who present to a non–PCI-capable facility ≥12 hours after onset of symptoms should be transferred to a PCI-capable facility when possible. However, if the patient has associated hemodynamic instability or a large infarct territory at risk, they are at very high risk for morbidity and death, and in this situation where timely PPCI is not possible, the benefits of fibrinolytic administration likely outweigh the benefit of prolonged transfer for PPCI.

Recommendation-Specific Supportive Text

1. PPCI is recommended to reduce the risk of MACE when FMC to PPCI can be achieved within 120 minutes. A patient who presents to a non–PCI-capable hospital with STEMI should be transferred to a PCI-capable hospital when this intervention can be accomplished within 120 minutes.[1,2,18] System delays related to transfer are frequently underestimated, and a case-by-case approach should be calculated for each patient with STEMI prior to transfer for PPCI.[19–21]
2. The use of fibrinolytic therapy in STEMI in the United States is driven by patients who are unable to receive timely PPCI (<120 minutes FMC to device activation). Numerous RCTs and meta-analyses have demonstrated superiority to PPCI over fibrinolytic therapy. However, the benefits of PPCI versus fibrinolytic therapy diminish with increasing PCI-related time delay such that after 120 minutes, the benefits are no longer as clear when compared with more timely fibrinolytic therapy administration.[19] In these patients, when timely PPCI cannot be performed, meta-analyses of RCTs and observational studies show statistically similar morbidity and mortality rates for a pharmaco-invasive approach (eg, fibrinolytic therapy followed by PCI within 2 to 24 hours) when a patient does not have timely access to PPCI.[4,5] The STREAM (Strategic Reperfusion Early After Myocardial Infarction) trial, which randomized 1892 early presenters (symptoms <3 hours) with STEMI unable to receive PCI within 1 hour of FMC, found that both a 30-day composite (eg, death, shock, CHF, or reinfarction) and 1-year mortality rates were similar for prehospital fibrinolysis versus transfer for PPCI.[10,22]
3. Small studies suggest that PPCI continues to offer clinical benefit in patients 12 to 24 hours after symptoms onset; therefore, transfer to a PCI-capable hospital is reasonable.[11,12] Late presenters with STEMI who have associated hemodynamic instability or large infarct size are at very high risk for acute deterioration and long-term morbidity. In this situation, fibrinolytic administration may outweigh potential risks when timely PPCI is not possible. Fibrinolysis in this setting should be followed by transfer to a PCI-capable center as soon as feasible.
4. There is no benefit of fibrinolysis and there is potential harm (eg, hemorrhagic stroke and major noncerebral bleeding) in administering fibrinolytic therapy to patients who present with symptoms concerning for ACS without ST-segment elevation or suspected true posterior STEMI.[13]

5.3.1. Timing and Choice of Agent for Fibrinolytic Therapy

Synopsis

PPCI remains the reperfusion modality of choice when it can be rapidly achieved in a patient with STEMI. In instances where this is not possible or cannot be achieved in a timely manner, the benefits of coronary reperfusion with fibrinolytic therapy in patients with STEMI are well established, with a time-dependent reduction in both mortality and morbidity rates during the initial 12 hours after symptom onset, especially in those who present early after symptom onset with low bleeding risk and large anterior infarctions.[1–7] The benefit of fibrinolytic therapy in patients who present >12 hours after symptom onset has not been established,[8–10] although consideration should be given to administering a fibrinolytic agent in symptomatic patients presenting >12 hours after symptom onset of STEMI with a large area of myocardium at risk or hemodynamic instability, if PCI is unavailable. Fibrin-specific fibrinolytic therapies are preferred over non–fibrin-specific agents due to superior patency rates and less immunogenicity (Table 13).[11–16] Tenecteplase is a genetically engineered version of alteplase with higher specificity for fibrin. In a large randomized trial of patients with AMI, tenecteplase and alteplase were equivalent for 30-day mortality rates, but tenecteplase was associated with reduced noncerebral bleeding.[17] Reteplase (re-

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Table 13. Fibrin-Specific Fibrinolytic Agents for STEMI

Fibrinolytic Agent	Dose
Tenecteplase (TNK-tPA)	Single IV weight-based bolus*
Reteplase (rPA)	Two 10-unit IV boluses given 30 min apart (administered over 2 min)
Alteplase (tPA)	90-min weight-based infusion†

Streptokinase is no longer available in the United States.

*30 mg for weight <60 kg; 35 mg for 60-69 kg; 40 mg for 70-79 kg; 45 mg for 80-89 kg; and 50 mg for ≥90 kg.

†Adults ≥67 kg: 100-mg total dosage administered as a 15-mg IV bolus, followed by 50-mg IV infused over 30 min, and then 35-mg IV infused over the next 60 min. Adults <67 kg: 15-mg IV bolus, followed by 0.75 mg/kg IV (not to exceed 50 mg) infused over 30 min, and then 0.5 mg/kg IV (not to exceed 35 mg) over the next 60 min.

rPA indicates reteplase plasminogen activator; TNK-tPA, tenecteplase tissue-type plasminogen activator; and tPA, tissue-type plasminogen activator.

combinant plasminogen activator) has not been shown to improve survival compared with alteplase in patients with MI, but its convenient bolus dosing allows for greater ease of use.[18] Adjunctive antiplatelet and/or anticoagulant therapies are indicated, regardless of the choice of fibrinolytic agent (Sections 4.3.2., "Oral P2Y12 Inhibitors During Hospitalization," and 4.4, "Parenteral Anticoagulation"). Absolute and relative contraindications for fibrinolytic therapy are listed in Table 14.

Patients should be transferred to a PCI-capable hospital after initiation of fibrinolytic therapy for routine coronary angiography (Section 5.3.2., "Coronary Angiography and PCI After Fibrinolytic Therapy"). Signs of failed reperfusion are discussed in Section 5.3.2.

5.3.2. Coronary Angiography and PCI After Fibrinolytic Therapy

Recommendations for Coronary Angiography and PCI After Fibrinolytic Therapy
Referenced studies that support recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
1	A	1. In patients with STEMI, transfer to a PCI-capable center immediately after fibrinolytic therapy is recommended.[1–5]
1	B-R	2. In patients with STEMI with suspected failed reperfusion after fibrinolytic therapy, immediate angiography with rescue PCI is recommended to reduce the risk of death or recurrent MI.*[6–9]
1	B-R	3. In patients with STEMI treated with fibrinolytic therapy, early angiography between 2 and 24 hours with the intent to perform PCI is recommended to reduce the rates of death or MI.*[1–5,10,11]

*Modified from the "2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization."[12]

Synopsis

Failure of reperfusion and risk of reocclusion after successful fibrinolytic therapy are important limitations of fibrinolytic therapy. For this reason, all patients receiving fibrinolytic therapy should be transferred to a PCI-capable hospital to facilitate immediate or early catheterization depending on the clinical circumstances. Hospitals should have transfer protocols in place to allow for a seamless transfer to the PCI-capable facility as soon as it is safe to do so. A detailed assessment of clinical status is critical to determine the timing of angiography. A lack of improvement in ischemic symptoms, persistent ST-segment elevation (<50% resolution of ST-segment elevation in the anterior leads or <70% in inferior leads [measured either from the lead with maximal baseline ST elevation or as the sum of ST-segment deviation across leads]),[13] or hemodynamic or electrical instability can indicate incomplete reperfusion by fibrinolytic therapy.[14] When there are signs of failed reperfusion, patients should undergo immediate coronary angiography and rescue PCI. For the remaining patients, routine coronary angiography within 2 to 24 hours after fibrinolytic therapy with coronary revascularization as needed is recommended.

Table 14. Absolute and Relative Contraindications for Fibrinolytic Therapy in STEMI*

Absolute Contraindications
Any prior ICH
Known structural cerebral vascular lesion (eg, arteriovenous malformation)
Known malignant intracranial neoplasm (primary or metastatic)
Ischemic stroke within 3 mo except acute ischemic stroke†
Suspected aortic dissection
Active bleeding or bleeding diathesis (excluding menses)
Significant closed-head or facial trauma within 3 mo
Intracranial or intraspinal surgery within 2 mo
Severe uncontrolled hypertension (unresponsive to therapy) (SBP >180 mm Hg or DBP >110 mm Hg)
Relative Contraindications
History of chronic, severe, poorly controlled hypertension
Significant hypertension on presentation (SBP >180 mm Hg or DBP >110 mm Hg)
History of prior ischemic stroke >3 mo
Dementia
Known intracranial pathology not covered in absolute contraindications
Traumatic or prolonged (>10 min) CPR
Major surgery (<3 wk)
Recent (within 2 to 4 wk) internal bleeding
Noncompressible vascular punctures
Pregnancy
Active peptic ulcer
Oral anticoagulant therapy

*Viewed as advisory for clinical decision-making and may not be all-inclusive or definitive.

†Acute ischemic stroke within 4.5 h of onset.

CPR indicates cardiopulmonary resuscitation; DBP, diastolic blood pressure; ICH, intracranial hemorrhage; SBP, systolic blood pressure; and STEMI, ST-segment elevation myocardial infarction.

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Recommendation-Specific Supportive Text

1. Numerous clinical trials have evaluated a strategy of early coronary angiography with possible PCI after fibrinolytic therapy. This strategy of immediate transfer and angiography has been associated with lower rates of recurrent ischemic events as compared with usual care.[1–5] Regardless of the timing of angiography, immediate transfer enables earlier access to specialized centers, providing critical care services and on-site catheterization laboratory teams that can facilitate clinical assessments to determine the likelihood of reperfusion and enable earlier angiography for the unstable patient.
2. Rescue PCI is associated with improved outcomes in patients with clinical signs of failed reperfusion after fibrinolytic therapy. Several trials have demonstrated a trend toward lower mortality and significantly lower rates of recurrent MI and HF when rescue PCI is performed for failed fibrinolysis.[6,7] The REACT (Rapid Early Action for Coronary Treatment) trial[6] enrolled 427 patients with failed reperfusion at 90 minutes after fibrinolysis to 1 of 3 treatment arms, including rescue PCI, conservative care, or repeat fibrinolytic therapy. Rescue PCI significantly reduced the composite primary endpoint of death, reinfarction, stroke, or severe HF at 6 months compared with either conservative care or repeat fibrinolytic therapy. Meta-analyses also support lower rates of death or reinfarction when rescue PCI is performed in this setting.[8,9] Minor and major bleeding and rates of stroke were significantly higher with rescue PCI.[6–8] These studies were performed in the era of femoral artery access, with fewer options for antiplatelet and anticoagulant therapy. The use of radial artery access[15] and the elimination of the routine use of glycoprotein IIb/IIIa inhibitors has reduced bleeding. For this reason, the balance of benefit from rescue PCI outweighs the risks for most patients with evidence of failed reperfusion after fibrinolysis.
3. Routine early angiography with the intent to perform PCI after fibrinolysis reduces MACE in comparison to usual care (delayed coronary angiography and/or an ischemia-guided strategy of revascularization).[1–5,11,16] In these studies, >80% of patients who were transferred underwent PCI to treat a significant residual stenosis or suboptimal flow of the infarct-related artery. Meta-analyses of the RCTs showed a reduction in the combined endpoint of death or reinfarction with an early invasive approach after fibrinolytic therapy.[10,17,18] In a network meta-analysis evaluating clinical outcomes with different modes of reperfusion for STEMI, a pharmaco-invasive strategy (defined as an interval between lysis and PCI ≥2 hours) was associated with a 21% reduction in the mortality rate when compared with a strategy of fibrinolysis alone.[18] Furthermore, contemporary registries have shown an association between a pharmaco-invasive approach and improved outcomes compared with PPCI when transfer times are long.[19] The optimal timing of angiography and PCI after fibrinolytic therapy has not been clearly defined but a similar benefit in ischemic endpoints is evident across the spectrum of times included in the clinical trials.[17,20] Although earlier studies raised concerns for increased bleeding with very early catheterization (mean time, 2.2 hours),[21] more contemporary data suggest similar rates of bleeding even if cardiac catheterization is performed very early after fibrinolytic therapy.[17,20]

6. NSTE-ACS: ROUTINE INVASIVE OR SELECTIVE INVASIVE INITIAL APPROACH

6.1. Rationale and Timing for a Routine Invasive or Selective Invasive Approach

Recommendations for Rationale and Timing for a Routine Invasive or Selective Invasive Approach
Referenced studies that support recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
Routine Invasive Versus Selective Invasive Strategy		
1	A	1. In patients with NSTE-ACS who are at intermediate or high risk of ischemic events and are appropriate candidates for revascularization, an invasive approach with the intent to proceed with revascularization is recommended during hospitalization to reduce MACE.*[1–6]
1	A	2. In patients with NSTE-ACS who are at low risk of ischemic events, either a routine invasive or selective invasive approach is recommended to help identify those who may require revascularization and to reduce MACE.[1–4,7]
Timing of Coronary Angiography for Those in Whom an Invasive Approach Is Planned		
1	C-LD	3. In patients with NSTE-ACS who have refractory angina or hemodynamic or electrical instability, an immediate invasive strategy with intent to perform revascularization is indicated to reduce MACE.†[8–11]
2a	B-R	4. In patients with NSTE-ACS who are at high risk‡ of ischemic events, it is reasonable to choose an early invasive strategy (within 24 hours) to reduce MACE.†[8,9,11,12]
2a	B-R	5. In patients with NSTE-ACS who are not at high risk and are intended for an invasive strategy, it is reasonable to perform angiography before hospital discharge to reduce MACE.*[8,11]

*Reproduced or
†modified from the "2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization."[7]
‡Predictors of risk are outlined in Figure 8.

Synopsis

A routine invasive approach refers to a strategy of performing coronary angiography with the intent to

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perform coronary revascularization by PCI or CABG (as appropriate) in patients with NSTE-ACS. This approach provides important prognostic information, including delineating the extent and severity of CAD. Several RCTs have demonstrated that a routine invasive approach in patients with NSTE-ACS reduces the risk of MACE when compared with a selective invasive approach.[1–3] Notably, these strategy trials were conducted in an era prior to the availability of hs-cTn assays, routine use of radial approach for coronary angiography, newer generation drug-eluting stents, and contemporary evidence-based antiplatelet therapies. Patients who are at prohibitively high risk from angiography or who have known coronary anatomy or preferences that preclude revascularization (PCI or CABG) may be managed noninvasively.[13] In addition, some low-risk patients, particularly those who have normal cardiac biomarkers and in whom a diagnosis of an ACS is questioned, should be considered for a "selective invasive" approach that includes further noninvasive risk stratification prior to consideration of coronary angiography, because they derive less benefit from a routine invasive approach.[4,7,13] These low-risk patients should still undergo noninvasive stress testing or coronary CT angiography prior to hospital discharge. Patients with higher risk findings on noninvasive testing or who have recurrent ischemic symptoms should be referred for invasive coronary angiography prior to hospital discharge in the absence of contraindication (Figure 7).

Recommendation-Specific Supportive Text

1. In patients with NSTE-ACS, a routine invasive approach improves clinical outcomes, including lower rates of recurrent MI and recurrent ischemia, compared with a selective invasive approach that involves further noninvasive risk stratification prior to consideration of angiography.[1–3] In a collaborative meta-analysis of RCTs, a routine invasive approach reduced death or MI by 18% (OR, 0.82 [95% CI, 0.72-0.93]), including a 25% reduction in MI (OR, 0.75 [95% CI, 0.65-0.88]) when compared with a selective invasive approach.[5] The benefit was more apparent in higher risk patients with elevated biomarkers.[4] The studies that established the benefit of a routine invasive approach were conducted in the late 1990s and early 2000s, and it is unknown whether contemporary

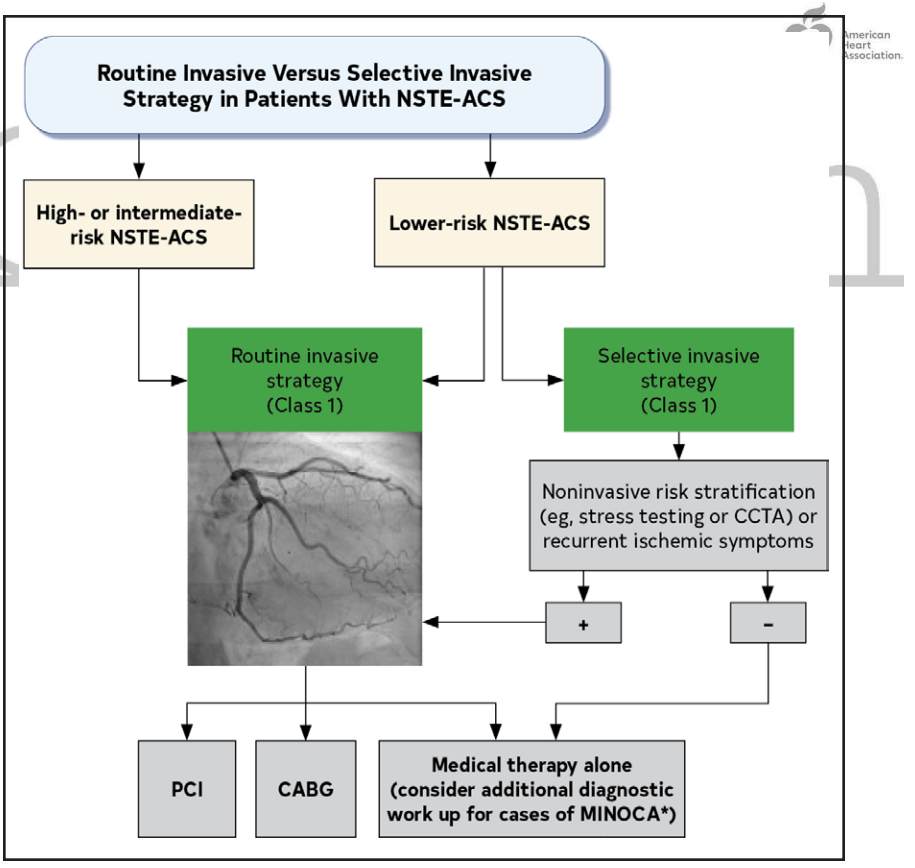
Routine Invasive Versus Selective Invasive Strategy in Patients With NSTE-ACS
High- or intermediate-risk NSTE-ACS
Lower-risk NSTE-ACS
Routine invasive strategy (Class 1)
Selective invasive strategy (Class 1)
Noninvasive risk stratification (eg, stress testing or CCTA) or recurrent ischemic symptoms
+
–
PCI
CABG
Medical therapy alone (consider additional diagnostic work up for cases of MINOCA*)

Figure 7. Selection of a Routine Invasive Versus Selected Invasive Strategy in Patients With NSTE-ACS.
Colors correspond to Class of Recommendation in Table 2. *AHA Scientific Statement on MINOCA.[17] CABG indicates coronary artery bypass grafting; CCTA, cardiac CT angiography; MINOCA, myocardial infarction with nonobstructive coronary artery disease; NSTE-ACS, non–ST-segment elevation acute coronary syndromes; and PCI, percutaneous coronary intervention.

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therapies and advances in interventional methods would yield different results. Similarly, elevated cardiac biomarkers (CK-MB and older generation troponin assays) identify those who benefit more from a routine invasive strategy; however, it remains unknown whether hs-cTn assays that detect smaller degrees of myonecrosis are as useful for identifying those who benefit from routine coronary angiography. Although women are less likely to have obstructive coronary disease at angiography, they derive as much benefit from a routine invasive approach in the presence of similar risk predictors.[4] The GRACE 2.0 risk calculator and TIMI Risk Score for unstable angina/NSTEMI may help identify patients at increased risk of MACE who benefit more from a routine invasive approach (Table 5).[1] Relative contraindications to coronary angiography that merit further consideration of the relative risks and benefits of a routine invasive approach are outlined in Table 15.

2. Although some trials have demonstrated a reduction in MACE with a routine invasive approach in NSTE-ACS,[1–3] others have not demonstrated a significant benefit when compared with a selective approach that involves further risk stratification.[4,7] Although a pooled analysis of 3 randomized trials suggested that the benefit of a routine invasive approach was independent of baseline risk,[6] other meta-analyses across studies have suggested that lower risk patients may derive less benefit.[4,5,14] In addition, some low-risk patients, particularly those who have normal cardiac biomarkers in whom a diagnosis of an ACS is suspect, may have improved outcomes with a selective invasive approach.[4,5] These patients should preferentially undergo noninvasive stress testing or coronary CT angiography prior to hospital discharge to help determine the need for coronary angiography; however, patients with suspected ongoing ischemic symptoms should be considered for coronary angiography.

Table 15. Relative Contraindications for a Routine Invasive Approach in ACS

High risk for bleeding on DAPT
Severe thrombocytopenia (platelet count <50 × 10^9/L)
Advanced kidney disease (not on dialysis)
Acute renal failure
Limited (<1-2 y) life expectancy
Advanced dementia
Known coronary anatomy that precludes PCI and/or CABG surgery
Patient preference

ACS indicates acute coronary syndromes; CABG, coronary artery bypass grafting; DAPT, dual antiplatelet therapy; and PCI, percutaneous coronary intervention.

3. Patients with NSTE-ACS who are unstable (eg, refractory or recurrent angina [despite optimal medical therapy, hemodynamic or electrical instability, acute pulmonary edema or HF, worsening mitral regurgitation]) have been largely excluded from RCTs. Despite a relative paucity of clinical trial data, these patients are at heightened risk of adverse outcomes, and an immediate invasive strategy (<2 hours from hospital admission) with intention to perform revascularization is recommended.[8,15] If patients with ACS and unstable features are at a non–PCI-capable hospital, they should be immediately transferred to a PCI-capable facility with a goal of immediate angiography. Clinical features that support immediate coronary angiography with intent to revascularize are listed in Figure 8.
4. For patients with NSTE-ACS for whom the decision has been made to proceed with coronary angiography, the benefit of an early invasive versus a delayed invasive approach is unclear.[8,9,11,12] In the TIMACS (Timing of Intervention in Acute Coronary Syndromes) trial,[11] patients were enrolled within 24 hours of symptoms and randomized to early angiography within 24 hours versus delayed angiography ≥36 hours from time of randomization. In the VERDICT (Very Early vs Deferred Invasive Evaluation Using Computerized Tomography) trial,[12] patients were randomized to early angiography within 12 hours versus delayed between 48 to 72 hours from time of diagnosis. Both studies reported no significant difference in MACE between an earlier versus delayed invasive approach in the overall study populations, but there was signal toward a reduction in MACE with an earlier invasive approach in the higher risk patients with a GRACE risk score >140.[11,12] In a meta-analysis of RCTs that compared an early versus delayed approach, a mortality benefit was not seen with earlier angiography. However, factors that favored an earlier invasive approach included a GRACE risk score >140, diabetes, age >75 years, and elevated cardiac biomarkers (although formal tests for interaction were not significant).[8] Although not evaluated in RCTs, a continuing steep rise in cardiac biomarkers, likely due to ongoing ischemia and myonecrosis despite optimized medical therapy, may also favor earlier coronary angiography.
5. In intermediate- or low-risk patients for whom angiography is planned in NSTE-ACS, timing does not appear to be critical, and a delayed invasive strategy within 48 to 72 hours does not appear to increase future risk of MACE.[8,10–12,15] Randomized trial data have not demonstrated an overall significant difference in death or MI between an earlier versus delayed invasive approach in nonselected patients with NSTEMI.[8,11,12,16]

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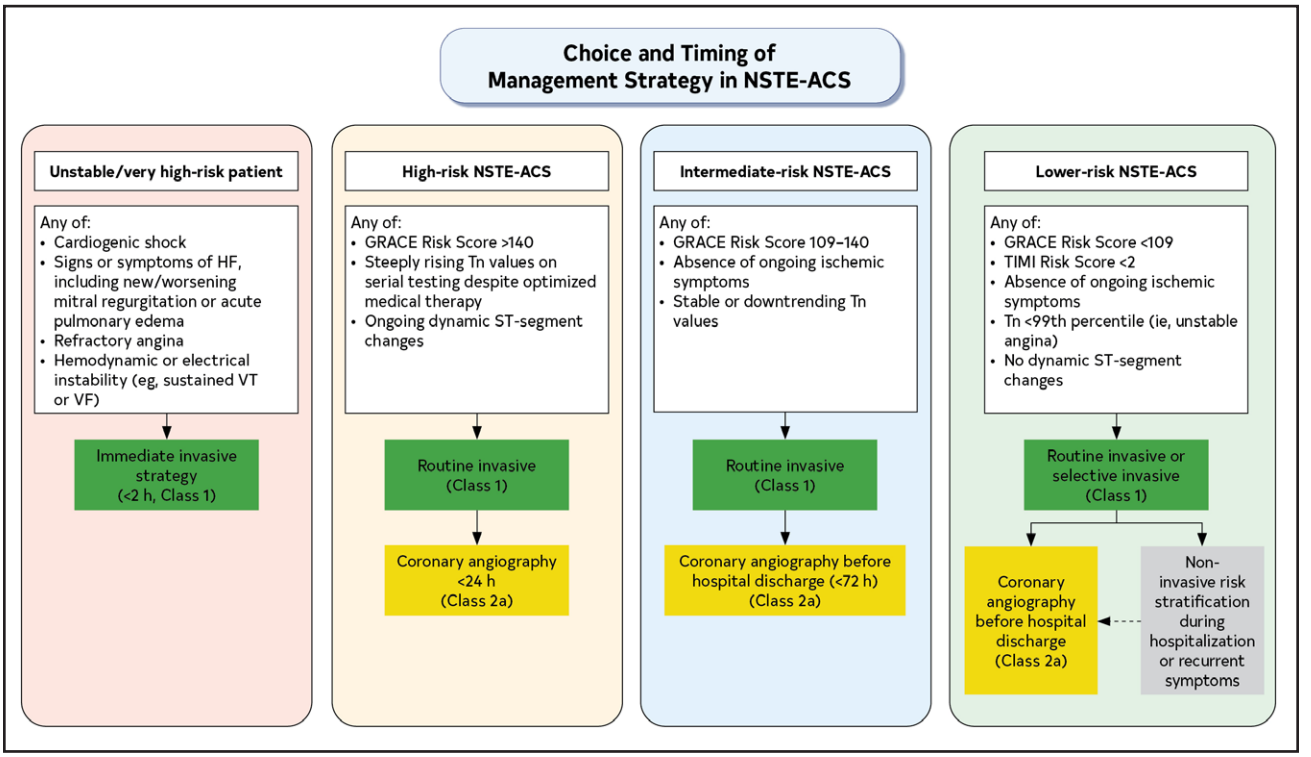
Choice and Timing of Management Strategy in NSTE-ACS
Unstable/very high-risk patient
Any of:
• Cardiogenic shock
• Signs or symptoms of HF, including new/worsening mitral regurgitation or acute pulmonary edema
• Refractory angina
• Hemodynamic or electrical instability (eg, sustained VT or VF)
Immediate invasive strategy (<2 h, Class 1)
High-risk NSTE-ACS
Any of:
• GRACE Risk Score >140
• Steeply rising Tn values on serial testing despite optimized medical therapy
• Ongoing dynamic ST-segment changes
Routine invasive (Class 1)
Coronary angiography <24 h (Class 2a)
Intermediate-risk NSTE-ACS
Any of:
• GRACE Risk Score 109–140
• Absence of ongoing ischemic symptoms
• Stable or downtrending Tn values
Routine invasive (Class 1)
Coronary angiography before hospital discharge (<72 h) (Class 2a)
Lower-risk NSTE-ACS
Any of:
• GRACE Risk Score <109
• TIMI Risk Score <2
• Absence of ongoing ischemic symptoms
• Tn <99th percentile (ie, unstable angina)
• No dynamic ST-segment changes
Routine invasive or selective invasive (Class 1)
Coronary angiography before hospital discharge (Class 2a)
Non-invasive risk stratification during hospitalization or recurrent symptoms

Figure 8. Selection and Timing of an Invasive Strategy in NSTE-ACS.
Figure 8 summarizes the recommendations in the 2025 ACS Guideline for a routine or selective invasive approach in NSTE-ACS. It is not meant to encompass every patient scenario or situation, and clinicians are encouraged to use a Heart Team approach when care decisions are unclear and to see the accompanying supportive text for each recommendation. Colors correspond to Class of Recommendation in Table 2. GRACE indicates Global Registry of Acute Coronary Events; HF, heart failure; NSTE-ACS, non–ST-segment elevation acute coronary syndromes; Tn, troponin; TIMI, Thrombolysis in Myocardial Infarction; VF, ventricular fibrillation; and VT, ventricular tachycardia. Adapted with permission from Lawton et al.[18] Copyright 2022 American Heart Association, Inc., and American College of Cardiology Foundation.

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7. CATHETERIZATION LABORATORY CONSIDERATIONS IN ACS

7.1. Vascular Access Approach for PCI

Recommendation for Vascular Access Approach for PCI Referenced studies that support recommendation are summarized in the Evidence Table.		
COR	**LOE**	**Recommendation**
1	A	1. In patients with ACS undergoing PCI, a radial approach is preferred to a femoral approach to reduce bleeding, vascular complications, and death.*[1–6]

*Modified from the "2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization."[7]

Synopsis

The radial artery has become the preferred vascular access site for patients undergoing cardiac catheterization and PCI.[8,9] Transradial access is associated with lower mortality, bleeding, and vascular complications in patients treated for ACS.[5] In addition, patients prefer radial access because it allows earlier ambulation and causes less discomfort than femoral access.[9] A caveat is most trials comparing radial versus femoral access had very low crossover rates because they required operators with expertise in radial access.[3] The choice of radial access has to be weighed against the possibility that the radial artery could be used as a bypass conduit for CABG surgery.[10] In sites where surgeons routinely utilize the radial artery as a bypass conduit, consideration should be given on the choice of vascular access and future use of radial artery for the cardiovascular surgical team. Although the radial artery is the most widely studied wrist access site, the use of alternative sites in the upper extremity, including the ulnar and distal radial arteries have yielded similar outcomes.[11,12] Transfemoral access, preferably with the use of ultrasound guidance, should be considered in patients in whom temporary MCS is planned and is the default alternative access site among patients in whom the radial artery cannot be used due to clinical, anatomical, or technical reasons.[13]

Recommendation-Specific Supportive Text

1. RCTs have consistently demonstrated the benefit of radial access in comparison with femoral access among patients treated for ACS. A meta-analysis using individual patient data from 7 high-quality RCTs (48.6% with NSTE-ACS; 46.2% with

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STEMI) demonstrated that radial access was independently associated with a significant 24% and 51% relative risk reduction of all-cause death and major bleeding, respectively, when compared with femoral access.[3] The magnitude of the mortality benefit was greater among patients with lower baseline hemoglobin levels. The benefit of radial access toward reducing bleeding was driven by a significant reduction in access-site bleeding. Vascular complications were significantly reduced by 62%. The MATRIX trial[6] demonstrated a significantly lower rate of the coprimary endpoints of MACE and net adverse clinical events (composites of death, MI, and stroke at 30 days, and MACE plus non-CABG major bleeding) among patients with ACS randomized to the transradial approach compared with the transfemoral approach. This is consistent with prior meta-analyses that have reported lower mortality and bleeding with radial access in patients with ACS.[4,14] The SAFARI-STEMI (Safety and Efficacy of Femoral Access versus Radial for Primary Percutaneous Intervention in ST-Elevation Myocardial Infarction) trial showed no difference in 30-day mortality rates between radial and femoral access; however, the trial stopped early and therefore was underpowered to detect a mortality benefit.[15]

7.2. Use of Aspiration Thrombectomy

Recommendation for Use of Aspiration Thrombectomy
Referenced studies that support recommendation are summarized in the Evidence Table.

COR	LOE	Recommendation
3: No benefit	A	1. Among patients with STEMI undergoing PPCI, manual aspiration thrombectomy should not be performed routinely prior to PCI given lack of clinical benefit.*[1–4]

*Modified from the "2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization."[5]

Synopsis

Despite restoration of coronary patency, suboptimal myocardial perfusion resulting from distal embolization or microvascular obstruction is frequent and is associated with larger infarct size, impairment of LV function, and excess mortality rates.[6,7] Removing coronary artery thrombus prior to balloon angioplasty, stent deployment, or both is an intuitive adjunct to PPCI that may yield putative clinical benefits. Routine manual thrombus aspiration performed via low profile catheters improved electrocardiographic and angiographic markers of myocardial perfusion in several clinical studies[8,9] and reduced adverse events in a single-center trial.[10,11] However, subsequent trials of manual aspiration thrombectomy have not demonstrated a clinical benefit.[1,2,4,12,13] Similarly, results from a pooled analysis showed that mechanical thrombectomy during STEMI was not superior to conventional PCI alone.

Recommendation-Specific Supportive Text

1. Results from several RCTs have shown that routine manual aspiration thrombectomy prior to PCI does not reduce MI size or improve clinical outcomes as compared with PCI alone.[1,2,4,12,13] In a patient-level, pooled analysis comprising 3 RCTs, aspiration thrombectomy did not reduce the primary endpoint of cardiovascular death at 30 days among patients with STEMI undergoing PPCI (n=18 306).[3] Similarly, aspiration thrombectomy did not lower risks for recurrent MI, target vessel revascularization, stent thrombosis, or HF at 30 days or 1 year. With respect to safety, the incidence of stroke or transient ischemic attack at 30 days and 1 year was numerically higher, albeit not statistically significant, among patients who underwent aspiration thrombectomy. Reductions in cardiovascular death were lower while risks for stroke or transient ischemic attack were higher among those with a large thrombus burden treated with aspiration thrombectomy. Dedicated studies are warranted to evaluate the role of selective aspiration thrombectomy in those high-risk patients most likely to benefit from thrombus removal prior to PCI. Manual aspiration thrombectomy may be performed as a bailout procedure to remove thrombus that persists after balloon angioplasty or stent deployment, particularly with concomitant no-reflow. Estimates from RCT cohorts indicate that 4% to 7% of patients with STEMI undergoing PPCI will require bailout aspiration thrombectomy.[1,2,10]

7.3. Use of Intracoronary Imaging

Recommendation for Use of Intracoronary Imaging
Referenced studies that support recommendation are summarized in the Evidence Table.

COR	LOE	Recommendation
1	A	1. In patients with ACS undergoing coronary stent implantation in left main artery or in complex lesions, intracoronary imaging with intravascular ultrasound (IVUS) or optical coherence tomography (OCT) is recommended for procedural guidance to reduce ischemic events.*[1–11]

*Adapted from the "2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization."[12]

Synopsis

Intracoronary imaging serves as a valuable tool for guiding the placement of coronary stents, particularly in cases involving the left main artery or complex lesions, resulting in greater stent expansion, less stent malapposition, and fewer coronary dissections.[1,2,4,13] IVUS provides a com-

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prehensive view of the vessel wall, allowing for the evaluation of plaque burden, calcification extent, lesion length, and external elastic lamina diameter before stent placement. It also facilitates the assessment of minimum stent area, malapposition, underexpansion, tissue protrusion, edge disease, and edge dissection after stent deployment.[14] OCT utilizes infrared light to produce high-resolution images of the vessel wall, offering specific advantages in assessing calcium thickness, lipid presence, thrombus formation, fibroatheroma, and plaque rupture, which is particularly helpful in patients with ACS. It is also useful for examining stent strut neointimal thickness, apposition, and edge dissections. However, it has limitations regarding imaging depth and requires the injection of contrast to clear blood, limiting its utility in cases of ostial left main disease. Both IVUS and OCT play essential roles in evaluating the necessity for lesion preparation, choosing the appropriate stent size, reducing the likelihood of geographical errors, confirming proper stent expansion, identifying complications, and determining the underlying reasons for stent failure.[14,15]

Recommendation-Specific Supportive Text

1. Randomized trials including patients with ACS have shown that intracoronary imaging guidance is associated with lower risk of target vessel failure (cardiac death, target vessel MI, or ischemia-driven target vessel revascularization) in patients undergoing PCI.[1–4] The advantages of intracoronary imaging are sustained over time and can be extended to less complex lesions.[5] Renovate-Complex PCI (Randomized Controlled Trial of Intravascular Imaging Guidance versus Angiography-Guidance on Clinical Outcomes after Complex Percutaneous Coronary Intervention) demonstrated a significant reduction in target vessel failure with intracoronary guidance (IVUS or OCT) versus angiographic guidance after a median follow-up of 2.1 years.[1] The OCTOBER (Optical Coherence Tomography Optimized Bifurcation Event Reduction) trial showed a significant reduction in target vessel failure at 2 years with OCT versus angiographic guidance in bifurcation lesions, including left main bifurcations.[4] Randomized trials directly comparing OCT versus IVUS have demonstrated that OCT is noninferior to IVUS for PCI-guidance.[6–8,10] However, the ILUMIEN IV: Optimal PCI (OCT Guided Coronary Stent Implantation Compared with Angiography) trial, the largest trial testing the strategy of imaging guidance with OCT, did not reveal a difference in target vessel failure with OCT in high-risk patients or patients with high-risk lesions; however, the coprimary endpoint of minimal stent area was significantly larger with OCT guidance compared with angiography guidance.[2] The rates of definite or probable stent thrombosis were also significantly lower with OCT-guided PCI compared with angiography-guided PCI. A minimum stent area of <4.5 to 5.0 mm^2 by OCT is considered to be an independent predictor of MACE.[16,17] Two large network meta-analyses showed that, in aggregate, intracoronary imaging guidance (with either IVUS or OCT) for PCI decreases cardiac death, target vessel MI, target lesion revascularization, and stent thrombosis.[11,18]

7.4. Management of Multivessel CAD in ACS

7.4.1. Management of Multivessel CAD in STEMI

Recommendations for Management of Multivessel CAD in STEMI
Referenced studies that support recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
1	A	1. In selected, hemodynamically stable patients with STEMI and multivessel disease (MVD), after successful PCI of the infarct-related artery, PCI of significantly stenosed* noninfarct-related arteries is recommended to reduce the risk of death or MI and improve angina-related quality of life (QOL).†[1–9]
2a	C-EO	2. In appropriate patients with STEMI and complex MVD, after successful PCI of the infarct-related artery, elective CABG surgery for significantly stenosed noninfarct-related arteries involving the left anterior descending artery or left main disease is reasonable to reduce the risk of cardiovascular events.†
2b	B-R	3. In selected hemodynamically stable patients with STEMI and low-complexity MVD (those not intended for CABG surgery), multivessel PCI of significantly stenosed noninfarct-related arteries at the time of PPCI may be preferred over a staged approach to reduce the risk of cardiovascular events.[10–12]
3: Harm	B-R	4. In patients with STEMI complicated by cardiogenic shock, routine PCI of a noninfarct-related artery at the time of PPCI should not be performed because of the higher risk of death or renal failure.*[13–15]

*Significantly stenosed refers to lesions that are severely diseased as defined by the "2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization" as a visually estimated diameter stenosis severity of ≥70% for non–left main disease and ≥50% for left main disease.[16]

†Modified from the "2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization."[16]

Synopsis

Several randomized trials of hemodynamically stable patients with STEMI have demonstrated that a strategy of multivessel PCI of significantly stenosed nonculprit vessels is safe and reduces risk of MACE when compared with PCI of the infarct-related artery alone.[1–8] These trials enrolled a select group of patients with anatomy suitable for PCI and without clinical factors precluding further invasive therapies. Recent studies suggest a lower risk of MACE (predominantly driven by a lower rate of recurrent ischemia and recurrent MI) when multivessel stent-

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ing occurs as a single procedure as opposed to when staged.[10–12] The decision to proceed with multivessel stenting and the timing of the procedure should take into account the patient's clinical and hemodynamic status, the duration and complexity of the infarct-related artery PCI, the complexity of disease in the noninfarct-related artery, the amount of myocardium in jeopardy, and the presence of comorbidities that might favor a conservative approach to care. Few studies of multivessel PCI have directly compared the efficacy of a physiologic-guided PCI versus an angiographic-guided PCI approach.[17,18] A meta-analysis across trials did not suggest any differential benefit for complete revascularization based on whether the approach was guided by fractional flow reserve (FFR) or angiography alone.[3]

Recommendation-Specific Supportive Text

1. Over the past decade, numerous trials have reported a significant reduction in MACE with complete revascularization.[1,2,4–8] These studies have demonstrated benefits to complete revascularization either at the time of PPCI[2,5–8] or as a staged procedure.[1,2,4,6] The PRAMI (Preventive Angioplasty in Acute Myocardial Infarction) trial,[8] one of the earliest trials of multivessel PCI, randomized 465 patients with STEMI and MVD to a strategy of complete revascularization versus culprit artery only revascularization. The trial was stopped early due to a significant reduction in the primary composite endpoint (cardiovascular death, nonfatal MI, or refractory angina) with complete revascularization, with significant reductions in nonfatal MI and refractory angina and a trend in reduction in the rates of cardiovascular death. The COMPLETE (Complete versus Culprit-Only Revascularization Strategies to Treat Multivessel Disease after Early PCI for STEMI) trial[1] randomized 4041 patients with STEMI and significant MVD to a strategy of staged PCI of the non–infarct-related artery (performed up to 45 days post MI) or culprit vessel–only revascularization with PCI reserved for patients with refractory symptoms. At a median follow-up of 3 years, multivessel PCI reduced cardiovascular death or MI and cardiovascular death, MI, or ischemia-driven revascularization. This benefit was consistent across all subgroups. Angina-related QOL was also significantly improved with multivessel PCI, with a greater proportion of patients in the complete revascularization arm who were angina-free in long-term follow-up.[9] In a meta-analysis, complete revascularization reduced cardiovascular death in patients with STEMI.[19] The benefits of complete revascularization with multivessel PCI should not be extrapolated to patients with disease more suited to CABG surgery, because they were excluded from these trials.
2. The trials examining the benefit of multivessel PCI in patients with STEMI and MVD excluded patients intended for CABG surgery. Furthermore, few patients with complex disease, such as chronic total occlusions or involvement of the left main artery, were included in these trials. For this reason, the benefits of a strategy of multivessel PCI cannot be extrapolated to patients with more complex noninfarct-related artery disease. In patients with CCD and complex CAD, including complex left main disease, or in patients with diabetes who have MVD involving the left anterior descending artery, CABG surgery is associated with improved event-free survival when compared with PCI.[20–24] As such, a similar benefit of CABG over PCI might be expected for patients with STEMI and complex non–infarct-related artery disease involving the left main or left anterior descending artery or in patients with diabetes and MVD involving the left anterior descending artery, who are stable and remote from their acute infarct, although the optimal timing of CABG is unclear in this setting and needs to take into account increased bleeding risk from DAPT.
3. Performing multivessel PCI at the time of PPCI offers the convenience of a single procedure, allowing for faster recovery, without the risk of repeated arterial access, or the potential for recurrent ischemia before the staged PCI. The BIOVASC (Direct Complete Versus Staged Complete Revascularization in Patients Presenting With Acute Coronary Syndromes and Multivessel Disease) trial[10] randomized 1525 patients with ACS (~40% with STEMI) and MVD to a strategy of a single setting immediate multivessel PCI or staged multivessel PCI. At 1 year, immediate multivessel PCI was noninferior to staged multivessel PCI for the primary endpoint all-cause death, MI, unplanned ischemia-driven revascularization, or cerebrovascular events. When compared with staged PCI, a single procedure multivessel PCI was associated with lower rates of recurrent MI and lower rates of unplanned ischemia-driven revascularization. The MULTISTARS AMI (Multivessel Immediate Versus Staged Revascularization in Acute Myocardial Infarction) study[11] compared a strategy of a single procedure multivessel PCI with staged multivessel PCI in 840 patients with STEMI and MVD. Immediate multivessel PCI was noninferior and superior to staged multivessel PCI for the primary endpoint of death, reinfarction, stroke, unplanned ischemia-driven revascularization, or hospitalization for HF at 1 year. This was largely driven by a lower rate of recurrent ischemia and recurrent infarction in the immediate group. In a network meta-analysis comparing all strategies for managing the non–infarct-related artery, a single

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procedure approach for immediate multivessel PCI was preferred followed by staged multivessel PCI.[12] Patients ideally suited for immediate complete revascularization include those with uncomplicated PCI of the infarct-related artery and low complexity noninfarct-related artery disease with stable hemodynamics, normal LV filling pressures, and normal renal function.

4. In patients with STEMI complicated by cardiogenic shock and MVD, a strategy of multivessel PCI is associated with worse outcomes.[13–15] The CULPRIT-SHOCK (Culprit Lesion Only PCI versus Multivessel PCI in Cardiogenic Shock) trial[13] randomized 706 patients with AMI, approximately 60% with STEMI, and cardiogenic shock to a strategy of complete multivessel PCI or culprit vessel–only PCI. At 30 days and 1 year, the rates of death or need for renal replacement therapy were significantly higher in the group of patients randomized to multivessel PCI.[13,14] Importantly, the CULPRIT-SHOCK trial only permitted enrollment if there was an identifiable culprit lesion. In situations where an unstable-appearing nonculprit artery lesion was observed, or in those patients with an uncertain culprit lesion, the decision to proceed with multivessel PCI may be more nuanced.

7.4.2. Management of Multivessel CAD in NSTE-ACS

Recommendations for Management of Multivessel CAD in NSTE-ACS Referenced studies that support recommendations are summarized in the Evidence Table.		
COR	**LOE**	**Recommendations**
1	**C-EO**	1. In patients with NSTE-ACS with MVD, the mode of revascularization (CABG or multivessel PCI) should be based on the disease complexity and patient's comorbidities.
Multivessel CAD and Candidates for PCI		
1	**B-R**	2. In stable patients with NSTE-ACS with MVD but without left main stenosis who are not intended for CABG surgery and undergoing culprit-lesion PCI, PCI of significant nonculprit lesions (at the time of the index procedure or as a staged procedure) is recommended to reduce the risk of MACE.[1–6]
2b	**B-R**	3. In patients with NSTE-ACS in whom multivessel PCI is being considered, physiological assessment of a nonculprit stenosis may be considered to guide revascularization decisions.[7–9]
3: Harm	**B-R**	4. In patients with NSTE-ACS complicated by cardiogenic shock, routine PCI of a nonculprit artery at the time of index procedure should not be performed because of the higher risk of death or kidney failure.*[10,11]

*Modified from the "2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization."[12]

Synopsis

Multivessel coronary disease, defined as angiographically significant stenosis (≥50%) in ≥2 epicardial arteries, is present in up to 40% to 70% of patients with NSTE-ACS. Identification of the culprit artery in these situations might be challenging.[13] Several subsets of patients, including those with complex left main disease, complex 3-vessel disease, and diabetes with left anterior descending artery involvement, might be appropriate for CABG surgery.[12] A Heart Team approach is recommended to consider CABG surgery versus multivessel PCI based on the complexity of CAD, technical feasibility, patient's surgical risk, and the potential for rehabilitation after CABG surgery. Dedicated RCTs comparing multivessel PCI versus culprit-only PCI exclusively among hemodynamically stable patients with NSTE-ACS are lacking. A large subgroup analysis from an RCT that included both patients with STEMI and NSTE-ACS and several observational studies have suggested that multivessel PCI among selected patients not intended for CABG reduces risk of MACE.[1–4,6,15] Angiographic assessment might overestimate the severity of a nonculprit lesion.[16] In one study, routine integration of physiological assessment of a nonculprit artery stenosis in NSTE-ACS led to change in management (ie, from revascularization to medical treatment only) in 38% of the cases.[17]

Recommendation-Specific Supportive Text

1. Studies evaluating the benefit of multivessel PCI among patients with NSTE-ACS and MVD excluded patients planned for CABG. The potential benefit of multivessel PCI cannot be extrapolated to patients with complex CAD. Indeed, certain subsets of patients might derive a survival benefit from CABG, including those with diabetes and disease involving the left anterior descending artery, left main with high complexity, MVD with complex or diffuse CAD, and those with severe LV dysfunction (Table 16).[18–21] Accordingly, a Heart Team approach is recommended to consider CABG surgery versus multivessel PCI based on the complexity of the CAD, technical

Table 16. Considerations for Choice of Coronary Revascularization Strategy for Patients With NSTE-ACS and MVD

In patients with NSTE-ACS and MVD, CABG surgery may be preferred over multivessel PCI in any of the following situations:
Significant left main coronary stenosis with high-complexity CAD
Multivessel CAD with complex or diffuse CAD
Diabetes mellitus and MVD with the involvement of the LAD
Multivessel CAD or complex left main CAD with severe left ventricular dysfunction

Adapted from the "2021 ACC/AHA/SCAI Coronary Revascularization Guideline."[12]

CAD indicates coronary artery disease; CABG, coronary artery bypass grafting; LAD, left anterior descending artery; MVD, multivessel disease; NSTE-ACS, non–ST-segment elevation acute coronary syndromes; and PCI, percutaneous coronary intervention.

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feasibility, patient's surgical risk, and the potential for rehabilitation after CABG surgery in these situations. In patients who are deemed appropriate for CABG, surgery could be considered prior to hospital discharge. Several observational studies have suggested that early CABG (performed within 3 days of presentation) may be associated with similar outcomes compared with delayed CABG.[22–24]

2. The FIRE (Functional Assessment in Elderly MI Patients With Multivessel Disease) trial enrolled 1445 elderly patients (median age, 80 years) with multivessel disease (ie, nonculprit artery with minimum vessel diameter >2.5 mm and angiography estimated stenosis 50% to 99%) and ACS (~65% with NSTE-ACS). Multivessel PCI reduced the risk of MACE, as well as reduced all-cause and cardiovascular mortality. The benefit was consistent between patients with NSTE-ACS versus patients with STEMI.[1] Several observational studies and a meta-analysis of observational studies demonstrated that multivessel PCI is associated with a lower incidence of long-term MACE.[2,3,6] Few RCTs have evaluated the optimal timing of a multivessel PCI approach. The SMILE (Single Staged Versus Multistaged PCI in Multivessel NSTEMI Patients) trial enrolled 584 patients and demonstrated that multivessel PCI conducted in a single procedure reduces risk of MACE at 1 year driven by a lower risk of revascularization.[4] The BIOVASC trial randomized 1525 patients with ACS (~60% with NSTE-ACS) and showed that multivessel PCI in a single procedure was noninferior to staged PCI with respect to MACE at 1 year and without evidence of an interaction between patients with NSTE-ACS versus patients with STEMI.[5,25]
3. In a secondary analysis including 328 patients with NSTE-ACS and MVD from the FAME (Fractional Flow Reserve Versus Angiography for Multivessel Evaluation) trial that randomized patients to either angiography-guided PCI (if diameter stenosis ≥50%) or FFR-guided PCI (if FFR ≤0.80), FFR-guided PCI reduced the number of stents and the incidence of MACE at 2 years.[7] The FRAME-AMI (Fractional Flow Reserve vs. Angiography-Guided Strategy for Management of Non-Infarction Related Artery Stenosis in Patients with Acute Myocardial Infarction) trial enrolled 562 patients with ACS and MVD (~53% with NSTE-ACS) and were randomized to FFR-guided PCI (if FFR ≤0.80) or angiography-guided PCI (diameter stenosis of >50%). FFR-guided PCI reduced the number of stents and the risk of MACE at 3.5 years with no evidence of interaction between patients with NSTE-ACS and patients with STEMI. Of note, the trial was prematurely terminated due to slow recruitment and enrolled <50% of the planned 1292 patients.[9] In the FAMOUS-NSTEMI (Fractional Flow Reserve Versus Angiographically Guided Management to Optimise Outcomes in Unstable Coronary Syndromes) trial, which randomized 350 patients with NSTE-ACS and MVD to FFR-guided PCI (if FFR ≤0.80) or angiography-guided PCI (diameter stenosis of >30%), FFR-guided PCI reduced the number of revascularization procedures at 1 year.[8]
4. In patients with NSTE-ACS complicated by cardiogenic shock and MVD, multivessel PCI at the time of the index procedure is associated with worse outcomes.[10,11] The CULPRIT-SHOCK (Culprit Lesion Only PCI versus Multivessel PCI in Cardiogenic Shock) trial randomized 706 patients with AMI and cardiogenic shock (approximately 40% with NSTE-ACS) to multivessel PCI at the time of the index procedure or culprit-only PCI. Multivessel PCI was associated with higher rates of death or need for renal replacement therapy at 30 days and at 1 year.[10,11] Notably, the CULPRIT SHOCK trial enrolled only patients with an identifiable culprit lesion. When there is an unstable-appearing nonculprit, or uncertain culprit, artery lesion, the decision to proceed with multivessel PCI will be based on the anatomic and clinical circumstances.

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8. CARDIOGENIC SHOCK MANAGEMENT

8.1. Revascularization in ACS With Cardiogenic Shock

Recommendations for Revascularization in ACS With Cardiogenic Shock
Referenced studies that support recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
1	B-R	1. In patients with ACS and cardiogenic shock or hemodynamic instability, emergency revascularization of the culprit vessel by PCI or with CABG is indicated to improve survival, irrespective of time from symptom onset.[1–4]
3: Harm	B-R	2. In patients with ACS complicated by cardiogenic shock, routine PCI of a noninfarct-related artery at the time of PPCI should not be performed because of the higher risk of death or renal failure.*[5–7]

*Modified from the "2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization."[8]

Synopsis

In patients with STEMI and hemodynamic instability, treatment delays to PPCI are associated with worse survival.[1] In patients with cardiogenic shock, PCI of

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the culprit vessel only is recommended.[5,6] Emergency CABG is recommended in those patients in whom PCI is not feasible.[2,9] Immediate revascularization with PCI or CABG is also recommended in high-risk patients with NSTEMI who are in cardiogenic shock.[2–5] The use of MCS devices in patients with cardiogenic shock is covered in Section 8.2, "MCS in Patients With ACS and cardiogenic shock."

Recommendation-Specific Supportive Text

1. In the SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) trial,[2] reported in 1999, patients with AMI and cardiogenic shock were randomized to medical therapy or emergency revascularization. Among the patients randomized to revascularization, 64% of patients were referred for PCI and 36% for CABG. The median time from randomization to revascularization was 0.9 hours for PCI and 2.7 hours for CABG. Despite lack of a significant difference in the primary endpoint of mortality at 30 days, emergency revascularization with either PCI or CABG reduced the mortality rate at 6 months,[2] and the mortality benefit was maintained through 1 and 6 years.[10,11] In an observational analysis from the FITT-STEMI (Feedback Intervention and Treatment Times in ST-Elevation Myocardial Infarction) trial, for every 10-minute delay in PPCI after 60 minutes from FMC, there were an additional 3 to 4 deaths per 100 with a >80% mortality rate beyond 6 hours of delay from FMC.[1] Therefore, it is recommended that PPCI should be performed in patients with STEMI and cardiogenic shock as soon as possible, ideally within 90 minutes, to reduce the mortality rate.[1,2] Observational studies suggest that emergency CABG remains a treatment option in patients with cardiogenic shock who are not amenable to primary reperfusion with PCI[3,4] or when PCI is unsuccessful.[4,12]
2. In patients with STEMI complicated by cardiogenic shock and MVD, a strategy of multivessel PCI is associated with worse outcomes.[5–7] The CULPRIT-SHOCK trial[5] randomized 706 patients with AMI (approximately 60% with STEMI) and cardiogenic shock to a strategy of complete multivessel PCI or culprit-only PCI. At 30 days and 1 year, the rates of death or need for renal replacement therapy were significantly higher in the group of patients randomized to multivessel PCI.[5,6] Importantly, the CULPRIT SHOCK trial permitted enrollment only if there was an identifiable culprit lesion. In situations where there is an unstable appearing nonculprit artery lesion, or in those patients with an uncertain culprit, the decision to proceed with multivessel PCI may be more nuanced.

8.2. MCS in Patients With ACS and Cardiogenic Shock

Recommendations for MCS in Patients With ACS and Cardiogenic Shock
Referenced studies that support recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
2a	B-R	1. In selected* patients with STEMI and severe or refractory cardiogenic shock, insertion of a microaxial intravascular flow pump is reasonable to reduce death.[1]
2a	B-NR	2. In patients with mechanical complication of ACS, short-term MCS devices are reasonable for hemodynamic stabilization as a bridge to surgery.[2–4]
3: No benefit	B-R	3. In patients with AMI and cardiogenic shock, the routine use of intra-aortic balloon pump (IABP) or venoarterial extracorporeal membrane oxygenation (VA-ECMO) is not recommended due to a lack of survival benefit.[5–9]

*See supportive text.

Synopsis

Cardiogenic shock is estimated to occur in approximately 10% of patients with STEMI and is associated with an early mortality rate of 40% to 50%.[10,11] Several types of devices for temporary MCS are available and have been studied in patients with cardiogenic shock with variable efficacy and increased risk of vascular complications. IABP counterpulsation improves coronary perfusion and reduces cardiac afterload. It is relatively easy to use and has a smaller insertion profile, which is associated with lower rates of vascular access site complications when compared with other MCS devices.[12,13] Percutaneous microaxial flow pumps unload the LV by draining blood from the LV and pumping it to the ascending aorta. They are dependent on adequate right ventricular function to fill the LV and require adequate oxygenation of blood. VA-ECMO provides both blood flow and oxygenation but increases afterload. Randomized trials of MCS devices remain challenging to conduct due to relative lack of equipoise on the part of treating physicians, leading to selective patient enrollment and limiting the generalizability of study results. Although small studies of microaxial flow pumps did not demonstrate clinical benefit for patients with AMI and cardiogenic shock,[14–16] a randomized trial at specialized centers in Europe demonstrated a mortality benefit with use of the microaxial flow pump in selected patients, albeit with increased risk of complications, including limb ischemia and renal replacement therapy.[1] Best practices for insertion of all MCS devices, including the multimodality use of fluoroscopy and ultrasound, should be utilized when feasible for obtaining femoral access.[17–19]

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Recommendation-Specific Supportive Text

1. The DanGer-SHOCK (Danish-German Cardiogenic Shock) trial enrolled patients with STEMI and cardiogenic shock of <24 hours duration, defined as hypotension (SBP <100 mm Hg or vasopressor support), end-organ hypoperfusion (arterial lactate ≥2.5 mmol/L and/or SvO_2 <55% with a normal PaO_2), and LVEF <45%. Patients who were comatose (Glasgow Coma Scale score <8) after out-of-hospital cardiac arrest and patients with overt right ventricular failure were excluded.[1] The study enrolled 360 patients at 14 specialized centers in Europe and randomized them to use of a microaxial flow pump or standard of care. Use of a microaxial flow pump significantly reduced the risk of all-cause mortality at 180 days by 26% (HR, 0.74 [95% CI, 0.55-0.99]; *P*=0.04; absolute risk reduction, 12.7%; number needed to treat =8) compared with standard of care. The absolute risk reduction seen in this trial is similar to the absolute risk reduction in 6-month mortality observed with emergency revascularization in patients with AMI and LV failure in the SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) trial.[1,20] However, given the increased risks of serious complications like bleeding, limb ischemia, and renal replacement therapy with the microaxial flow pump seen in the DanGer Shock trial, the COR is based on the balance between these risks and the reduction in death. Additionally, the timing of microaxial flow pump placement was not dictated by the trial protocol; thus, the preferred timing of placement is unclear. Based on these results, use of a microaxial flow pump is reasonable to reduce mortality in patients with STEMI and cardiogenic shock who have clinical features consistent with the inclusion criteria of the DanGer-SHOCK trial. In particular, patients with STEMI who present with SCAI shock stages C, D, or E, who are noncomatose and have adequate peripheral vasculature to accommodate large-bore access are reasonable candidates for the microaxial flow pump.
2. Although randomized trial data are lacking, MCS devices can be considered as a bridge to surgery for patients with mechanical complications of AMI when adequate clinical stabilization is required and may allow for further tissue stabilization at the injured site. A systemic review of patients treated with MCS as a bridge to surgical treatment of ventricular septal rupture yielded 111 studies (n=2440) with almost all patients receiving initial IABP support (n=2263).[2] Of the 129 patients who underwent additional MCS device placement (77.5% of whom were on VA-ECMO), the lowest in-hospital mortality was observed in those treated with VA-ECMO (29.2%) when compared with those treated with an IABP alone (52.0%). However, 2 database analyses that were not included in the systematic review demonstrated higher in-hospital death with use of VA-ECMO in patients with post-AMI mechanical complications.[3,4] Evaluation of the ECLS (Extracorporeal Life Support) Organizations Registry yielded 158 patients with post-AMI mechanical complications who underwent VA-ECMO.[3] Survival to hospital discharge here was low at 37.3%, and complications related to VA-ECMO use occurred in 75.3% of patients. Evaluation of the National Inpatient Sample yielded 10 726 patients with post-STEMI mechanical complications, and the use of VA-ECMO was associated with increased in-hospital mortality (OR, 2.80 [95% CI, 1.92-4.04]), while the use of an IABP was not associated with lower mortality.[4] Both data sources included use of VA-ECMO at any time during the hospitalization for post-AMI mechanical complications, including use of VA-ECMO postsurgery, a cohort at highest risk of in-hospital mortality.
3. The IABP-SHOCK II (Intraaortic Balloon Pump in Cardiogenic Shock II) trial randomized patients with AMI and severe or refractory cardiogenic shock in whom early revascularization was planned to IABP or no IABP.[5] At 30 days and long-term follow-up, no differences were observed in the primary outcome of all-cause death or the secondary biomarker or measures of disease severity endpoints.[6,7] VA-ECMO has not been shown to reduce death compared with medical therapy alone in patients with cardiogenic shock in the setting of MI but increases major bleeding and vascular complications.[21] The ECMO-CS (Extracorporeal Membrane Oxygenation in the Therapy of Cardiogenic Shock) trial randomized patients with rapidly deteriorating or severe cardiogenic shock to immediate or no immediate VA-ECMO.[8] At 30 days, no differences were observed in the primary composite endpoint of all-cause death, resuscitated cardiac arrest, and implementation of another MCS device with results consistent in the 74 patients with cardiogenic shock related to MI and in the as-treated analysis. The ECLS-SHOCK (Extracorporeal Life Support in Infarct-Related Cardiogenic Shock) trial randomized patients with AMI and severe or refractory cardiogenic shock in whom early revascularization was planned to early ECLS or no ECLS.[9] No differences were observed in the primary outcome of the 30-day mortality rate or secondary outcomes. Moderate or severe bleeding and peripheral vascular complications

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requiring intervention were higher in the ECLS versus no ECLS group. Overall, these studies do not support routine use of IABP and VA-ECMO in patients with AMI and cardiogenic shock.

9. ACS COMPLICATIONS

9.1. Mechanical Complications

Recommendations for Mechanical Complications
Referenced studies that support recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
1	C-EO	1. Patients with a mechanical complication of ACS should be managed in a facility with cardiac surgical expertise.
2a	B-NR	2. In patients with a mechanical complication of ACS, short-term MCS devices are reasonable for hemodynamic stabilization as a bridge to surgery.[1–3]

Synopsis

Timely reperfusion therapy has reduced the incidence of mechanical complications (ventricular septal rupture, mitral valve insufficiency due to papillary muscle infarction or rupture, or free wall rupture) after AMI (Figure 9).[3,5] Although occasionally found incidentally, mechanical complications commonly present with recurrent or refractory chest pain or a new murmur accompanied by disproportionate HF, cardiogenic shock, or sudden cardiac death on clinical presentation within the first week after an AMI. Medical therapy alone is associated with high risk of early death[6,7]; definitive surgical correction is frequently the treatment of choice.[8,9] Mortality rates with surgery are highest in subjects with cardiogenic shock and in those requiring early emergency/urgent intervention after AMI.[10,11] Observed mortality rates following delayed surgery (>7 days) are lower but patient selection and survivor bias contribute to this observation.[12,13] The availability of temporary MCS devices has led to increasing trends for delayed surgery due to concerns for the initial degree of extensive tissue destruction.[14,15] Delayed surgical intervention may enable hemodynamic stabilization, lead to recovery of end-organ injury, and promote infarct tissue healing and maturation that could facilitate definitive repair. Percutaneous approaches toward repair have been used in patients with prohibitive surgical risk or contraindications to surgery as a primary or temporizing option in the setting of acute mitral regurgitation and ventricular septal rupture and remain an evolving area of investigation.[16,17] Select patients with mechanical complications of ACS may be considered for cardiac transplantation or durable left ventricular assist device as a primary or bailout treatment strategy to improve survival.[18]

Recommendation-Specific Supportive Text

1. No RCTs evaluate the role of transfer of patients with mechanical complications after MI to dedicated centers with cardiac surgical expertise. Although overall surgical mortality is approximately 40%, it remains the treatment strategy of choice. Hemodynamic deterioration is unpredictable and can be precipitous in previously stable subjects. Consequently, transfer to a Level 1 cardiac intensive care unit (CICU)[19] with access to various temporary MCS devices and multidisciplinary experienced teams of surgical, interventional, HF, and palliative care specialists is recommended. Emerging data following the creation of shock teams supports the transfer of hemodynamically unstable patients from community hospitals to centers with multidisciplinary expertise.[20,21] Although the exact timing remains uncertain, early corrective surgery is the treatment of choice for mechanical complications of MI.[8,9,13] The risk of surgical correction is highest when performed in the setting of cardiogenic shock[10,22,23] and appears lower when surgery is delayed. The early hazard with surgery is attributed to patient acuity, end-organ injury, and lack of tissue integrity to promote definitive and lasting repair. Selected subjects may be candidates for either definitive or temporizing percutaneous structural intervention as a bridge to definitive surgical intervention.[16,17,24] Given the complexity of decision making, a Heart Team approach to guide feasibility, timing, and nature of corrective intervention as well as the need and selection of MCS support is recommended as soon as a mechanical complication is diagnosed.
2. No RCTs have evaluated the role of MCS in improving clinical outcomes in the setting of mechanical complications. The choice of specific MCS should be individualized and guided by patient characteristics, nature of the mechanical complication, and the hemodynamic profile. In patients with ventricular septal rupture, the use of an IABP has been shown to reduce left-to-right shunting and improve hemodynamics in patients with and without shock.[25] Favorable hemodynamic effects with IABP are also noted with acute ischemic mitral regurgitation. Various devices have been utilized when IABP fails or if hemodynamic instability remains profound.[1] The use of MCS devices has enhanced hemodynamic stabilization to allow the opportunity for consideration of delayed corrective strategy.[14,15]

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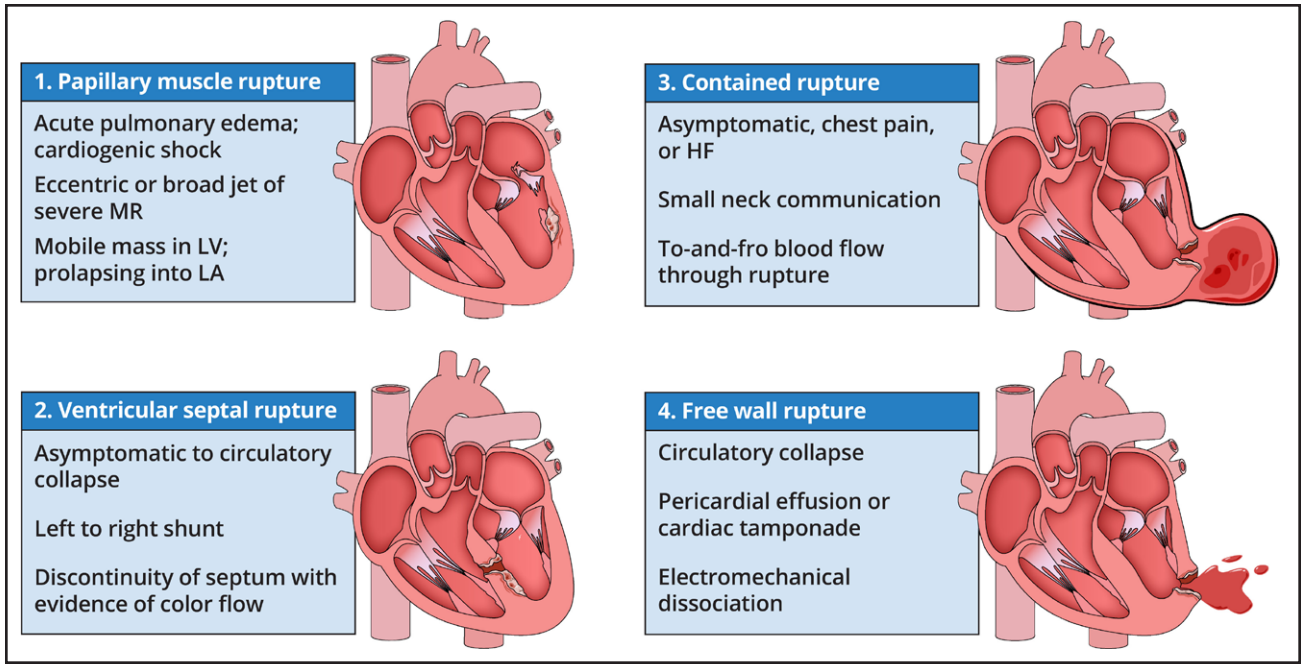
1. Papillary muscle rupture
Acute pulmonary edema; cardiogenic shock
Eccentric or broad jet of severe MR
Mobile mass in LV; prolapsing into LA
3. Contained rupture
Asymptomatic, chest pain, or HF
Small neck communication
To-and-fro blood flow through rupture
2. Ventricular septal rupture
Asymptomatic to circulatory collapse
Left to right shunt
Discontinuity of septum with evidence of color flow
4. Free wall rupture
Circulatory collapse
Pericardial effusion or cardiac tamponade
Electromechanical dissociation

Figure 9. Clinical Characteristics of Mechanical Complications of Acute Myocardial Infarction.
Contained rupture is the preferred term for an entity sometimes referred to as pseudoaneurysm. HF indicates heart failure; LA, left atrium; LV, left ventricle; and MR, mitral regurgitation. Modified with permission from Damluji et al.[26] Copyright 2025 Devon Medical Art.

9.2. Electrical Complications and Prevention of Sudden Cardiac Death After ACS

Recommendations for Electrical Complications and Prevention of Sudden Cardiac Death After ACS
Referenced studies that support recommendations are summarized in the Evidence Table.

COR	LOE	Recommendations
Ventricular Arrhythmias		
1	A	1. In patients post MI, implantable cardioverter-defibrillator (ICD) implantation is recommended in selected patients with an LVEF ≤40% (Table 17) at least 40 days post MI and at least 90 days postrevascularization to reduce death.*[1–4]
2a	C-EO	2. In patients post ACS, ICD implantation is reasonable in patients with clinically relevant ventricular arrhythmias >48 hours and within 40 days post MI to improve survival.*[5,6]
2b	B-R	3. In patients early after MI, usefulness of a temporary wearable cardioverter-defibrillator is uncertain in patients with an LVEF ≤35% to improve survival.[7]
Bradyarrhythmias		
1	B-NR	4. In patients presenting with an AMI with sustained evidence of second-degree Mobitz type II atrioventricular block, high-grade atrioventricular block, alternating bundle-branch block, or third-degree atrioventricular block (persistent or infranodal), permanent pacing is indicated.†[8,9]

*Adapted from the "2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death."

†Adapted from the "2018 ACC/AHA/HRS Guideline on the Evaluation and Management of Patients With Bradycardia and Cardiac Conduction Delay."

Synopsis

Electrical complications in patients with ACS may create challenges in clinical management due to consideration for the need of anticoagulant therapy in patients who develop atrial fibrillation (AF) or flutter and possible need for antiarrhythmic therapy and electrophysiologic interventions. Many of these considerations have been addressed in depth in separate guideline documents.[10] Generally, arrhythmic complications increase both morbidity and mortality rates in patients after ACS. Patients who present with AMI with reduced LVEF (≤40%) have increased risk of new-onset AF, bradyarrhythmias, and ventricular arrhythmias.[11,12] This risk appears to be increased in those patients who are not revascularized or receive fibrinolytic therapy compared with those who undergo PCI.[11]

Recommendation-Specific Supportive Text

1. Ventricular arrhythmias are common after ACS and more common in patients with reduced LVEF. MADIT II (Multicenter Automatic Defibrillator Implantation Trial) demonstrated a 31% reduction in all-cause mortality (HR, 0.69 [95% CI, 0.51-0.93]) for prophylactic implantation of a cardiac defibrillator in patients with an LVEF ≤30% who were at least 30 days after MI or 3 months after revascularization for MI and had an anticipated life expectancy longer than 1 year.[2] A mortality benefit

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Table 17. LVEF and Patient Characteristics Defining an Indication for Prophylactic ICD Implantation for Primary Prevention in Ischemic Heart Disease

LVEF	Patient Category: All Patients Should Have Expected Survival of ≥1 y
≤30%	NYHA class I, II, or III[2]
31%-35%	NYHA class II or III[1,3]
≤40%	Inducible VT[1,4,13]

ICD indicates implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; and VT, ventricular tachycardia.

for prophylactic ICD implantation has also been shown in patients with an LVEF ≤35% and New York Heart Association class II or III HF symptoms,[1,3] as well as in patients with inducible ventricular tachycardia or ventricular fibrillation and an LVEF ≤40%[1,4,13] (Table 17).

2. The risk of ventricular arrythmias and sudden cardiac death is highest early after MI, although the routine implantation of a defibrillator (for primary prevention) in patients with LV dysfunction early after MI or CABG has not been associated with improved survival.[14–16] In DINAMIT (Defibrillator in Acute Myocardial Infarction Trial), ICD implantation led to a 58% reduction in arrhythmic deaths within 6 to 40 days post MI with ejection fraction ≤35%; however, this was offset by an increase in nonarrhythmic deaths.[16] Sustained episodes of ventricular tachycardia or ventricular fibrillation occurring >48 hours after reperfusion are associated with an increased risk of death,[12,17] and the risk of sudden cardiac death is highest in the first month.[5] Patients with ventricular arrhythmias should first be managed with beta blockers and/or antiarrhythmic therapy. The benefit of ICD implantation in patients with persistent or sustained ventricular arrhythmias and who are <40 days post MI remains unclear.[15,16,18] A single-center observational study enrolled patients post STEMI (median, 9 days) and referred those with an LVEF ≤40% for electrophysiologic testing and implanted an ICD only in those with inducible ventricular tachycardia. Although a randomized comparator arm was unavailable, 22% of those who underwent ICD implantation had ventricular tachycardia terminated by the device during the first 12 months.[6] The effects of ICD implantation on mortality cannot be definitely ascertained, and more research is required. Radiofrequency catheter ablation should be considered in patients with recurrent ventricular tachycardia or ventricular fibrillation followed by ICD implantation.[19] Earlier ICD implantation can be considered in patients who have an indication for a permanent pacemaker prior to hospital discharge and in whom LVEF is not expected to recover, but no evidence was observed to definitively demonstrate the safety of this approach.[10,20]
3. In the VEST (Vest Prevention of Early Sudden Death) trial, the routine use of a temporary wearable cardioverter-defibrillator did not significantly reduce the primary endpoint (composite of sudden death or death from ventricular tachyarrhythmias at 90 days) in patients with AMI and LVEF ≤35% (relative risk, 0.67 [95% CI, 0.37-1.21]).[7,21] The secondary endpoint of death from any cause was lower in the wearable vest group compared with the no-device group (relative risk, 0.64 [95% CI, 0.43-0.98]); only 12 of 48 patients were wearing the device at the time of death.[7] Greater benefit was demonstrated in those who were compliant with the device.[21] As such, use of a wearable cardioverter-defibrillator could be considered in high-risk patients with reduced LVEF as a bridge to consideration for the need for an ICD.
4. Patients with STEMI with second- or third-degree atrioventricular block have higher in-hospital mortality than those without high-degree atrioventricular block.[22,23] Patients who present with ACS with complete heart block have a higher incidence of cardiogenic shock, ventricular arrhythmia, and death.[24,25] In a contemporary cohort of patients with AMI, the incidence of high-degree atrioventricular block has decreased from 4.2% to 2.1%; however, increased morbidity and mortality remain despite reperfusion therapy in those with high-degree atrioventricular block.[26,27] A pooled analysis of 30 000 patients found that high-degree atrioventricular block, asystole, and electromechanical dissociation are infrequent complications of NSTEMI but are associated with increased short-term mortality. High-degree atrioventricular block is not considered to be responsible for the increased mortality but is a surrogate marker of larger infarct size.[28] Temporary pacemaker insertion in the setting of ACS in patients with high-degree atrioventricular block and other pacer indications has been found to improve postdischarge survival.[8,9,29] Permanent pacemaker insertion is recommended with unresolved high-degree atrioventricular block that persists >72 hours.[20]

9.3. Pericarditis Management After MI

Synopsis

The diagnostic criteria for post-MI pericarditis are displayed in Table 18. Pericarditis that occurs early after MI typically arises 1 to 3 days after a transmural event and is presumed to be inflammatory in nature due to adjacent myocardial necrosis. These cases of early pericarditis are typically transient, lasting several days, and will resolve

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Table 18. Clinical Criteria for Diagnosis of Pericarditis

Diagnosis Is Made With Presence of Pleuritic Chest Pain and ≥1 of the Following Criteria:
Friction pericardial rub on auscultation
Electrocardiographic evidence such as classic PR-segment depression or diffusive concave ST-segment elevations, or in the setting of MI, persistent ST-segment elevations or dynamic T-wave changes
New or growing pericardial effusion on echocardiography

MI indicates myocardial infarction.

with conservative therapy. Acetaminophen can be given for symptomatic relief. A second form of pericarditis may occur weeks after MI (Dressler's syndrome) and is believed to be immune-mediated as a response to pericardial irritation or damage, such as in the setting of any degree of hemopericardium.[1,2] These cases of late pericarditis often require additional therapy (Table 19). Given the rarity of post-MI pericarditis (0.1%-0.5%) in the era of early coronary reperfusion therapy,[3] dedicated RCTs of high-dose aspirin are lacking, and data are extrapolated from studies of the heterogeneous diagnosis of acute pericarditis.[4] Furthermore, RCTs of colchicine were performed on a background of high-dose aspirin therapy.[5–7] If symptoms persist despite standard supportive therapy in early pericarditis and in any late pericarditis, high-dose aspirin may be used to reduce symptoms.[4] The use of colchicine should also be considered to reduce symptoms and decrease risk of recurrence[8,9]; suggested dosing is summarized in Table 19. The value of a loading dose of colchicine in this setting is unclear. Routine use of high-dose aspirin or colchicine is not indicated for the management of asymptomatic pericardial effusions.[10,11] Glucocorticoids and nonsteroidal anti-inflammatory drugs (other than aspirin) are potentially harmful due to possible increase in risk of recurrent MI or impaired myocardial healing and risk of rupture.[12,13]

9.4. Management of LV Thrombus After MI

Synopsis

LV thrombus typically occurs in the setting of large anterior STEMI and can lead to thromboembolic complications, including stroke and systemic embolization. In the era of PCI, the incidence of LV thrombus after ACS has decreased and is estimated to be <5% to 10% in the post-MI population.[1–3] Limited RCT data are available on the contemporary management of LV thrombus, and current management is based mostly on retrospective and observational data and expert consensus. Patients at highest risk for LV thrombus include those with anterior STEMI involving the left anterior descending artery, LVEF <30% (especially in the presence of an LV aneurysm), and longer times to reperfusion. An echocardiogram is the recommended imaging modality for diagnosis, given its wide accessibility and low cost.[4] Cardiac MRI is more sensitive for detection of LV thrombus and may be considered when there is high clinical suspicion and echocardiogram results are inconclusive. LV thrombus may form later during hospitalization or after discharge; therefore, repeat imaging can sometimes detect LV thrombus in high-risk patients.[5] Because DAPT is recommended for most patients early after ACS, the addition of an anticoagulant for LV thrombus needs to be considered in the context of the patient's overall bleeding risk versus their risk of an embolic event. Most patients with LV thrombus will warrant anticoagulation for a period of 3 months, at which time the presence of residual thrombus can be assessed by repeat imaging to help determine whether a more prolonged course is warranted.[1] Although direct oral anticoagulants (DOAC) are routinely used in clinical practice, there are limited data comparing the efficacy of a DOAC versus vitamin K antagonist in the setting of LV thrombus. Observational studies and small RCTs have suggested that DOAC may be noninferior to vitamin K antagonist with respect to mortality, stroke, or LV thrombus resolution, and DOACs may offer an improved bleeding profile.[6] The practical management of LV thrombi is more completely addressed in other documents.[1,6]

Table 19. Additional Therapy for Persistent/Late Pericarditis Symptoms

Medical Therapy	Dosing Schedule
High-dose aspirin	500-1000 mg every 6-8 h until symptoms improve
Colchicine	0.5-0.6 mg once* or twice daily for 3 mo

*Daily dosing should be used in patients who weigh <70 kg and further adjusted in patients with stage 4-5 kidney disease, severe hepatic impairment, or with concomitant P-glycoprotein and/or moderate and severe CYP3A4 inhibitors.

10. IN-HOSPITAL ISSUES IN THE MANAGEMENT OF ACS

10.1. Cardiac Intensive Care Unit

Recommendation for CICU		
COR	**LOE**	**Recommendation**
1	C-EO	1. Patients with ACS and with ongoing angina, hemodynamic instability, uncontrolled arrhythmias, suboptimal reperfusion, or cardiogenic shock should be admitted to a CICU to reduce cardiovascular events.

Synopsis

The nurse-to-patient ratio in the CICU should be sufficient to provide (1) continuous electrocardiographic rhythm monitoring, (2) frequent assessment of vital signs and mental status, and (3) ability to perform rapid cardioversion and defibrillation for arrhythmias.[1,2] Some hospitals may not have a dedicated CICU but rather care for patients with MI within a general multipurpose ICU; this approach requires trained providers with sufficient expertise in the care of cardiac patients.

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Recommendation-Specific Supportive Text

1. Admission to the CICU and optimal length of stay in the CICU after an MI should be based on patients' risk profile and clinical stability, while considering the patient's baseline cardiac risk and comorbidities. Patients with ACS with continuing/ongoing angina, hemodynamic instability, uncontrolled arrhythmias, or a large MI with HF, cardiogenic shock, or both, should be admitted to a CICU.[1,2] Patients with ongoing ischemic symptoms should be preferentially triaged for cardiac catheterization whenever possible. Stable patients with ACS and without recurrent ischemia, significant arrhythmias, pulmonary edema, or hemodynamic instability do not need CICU admission and can be admitted to an intermediate care or telemetry unit. Clinical predictors may be useful for helping identify patients who will require CICU care. For example, the ACTION ICU risk score for CICU admission integrates 9 variables on presentation to the ED including: signs or symptoms of HF, initial heart rate, initial SBP, initial troponin, initial serum creatinine, prior revascularization, chronic lung disease, ST-segment depression, and age >70 years.[3]

10.2. Management of Anemia in ACS

Recommendation for Management of Anemia in ACS Referenced studies that support recommendation are summarized in the Evidence Table.		
COR	**LOE**	**Recommendation**
2b	**B-R**	1. In patients with ACS and acute or chronic anemia, blood transfusion to achieve a hemoglobin level ≥10 g/dL may be reasonable to reduce cardiovascular events.[1]

Synopsis

Anemia is common in patients with ACS and is associated with worse short- and long-term outcomes.[2–4] Anemia is associated with adverse outcomes irrespective of whether the anemia is chronic and due to comorbid conditions, or acute and the result of bleeding related to antithrombotic therapy and/or invasive procedures. The adverse effects of anemia may be due to decreased myocardial oxygen delivery, increased myocardial oxygen demand due to increased cardiac output, or the avoidance of potentially beneficial antithrombotic drugs and/or procedures. In observational studies, blood transfusion has been associated with worse clinical outcomes.[5–8] Randomized trials in medically ill patients and those undergoing cardiac surgery have demonstrated similar or better outcomes with a restrictive transfusion strategy (targeting a blood hemoglobin level around 8 g/dL) than with a liberal transfusion strategy (targeting a blood hemoglobin level around 10 g/dL).[9–11] However, randomized trial evidence for populations with ACS suggests possible clinical benefit for a more liberal transfusion strategy targeting a hemoglobin level above 10 g/dL compared with targeting a hemoglobin level above 7 g/dL to 8 g/dL.[1,12,13]

Recommendation-Specific Supportive Text

1. The MINT (Myocardial Ischemia and Transfusion) trial randomly assigned 3504 patients with acute STEMI or NSTEMI and anemia with a blood hemoglobin level of <10 g/dL (13% with recent bleeding) to a restrictive transfusion strategy (transfusing if the hemoglobin level was <7-8 g/dL) or a liberal transfusion strategy (transfusing if the hemoglobin level was <10 g/dL).[1] Patients were ineligible for enrollment if they had uncontrolled bleeding, were receiving palliative treatment, or were scheduled to have cardiac surgery. Transfusion could be delayed for patients with volume overload or until day of dialysis in patients with end-stage renal disease. The primary outcome of 30-day death or recurrent MI occurred in 16.9% of patients in the restrictive strategy and 14.5% of patients in the liberal strategy (relative risk, 1.15 [95% CI, 0.99-1.34]; *P*=0.07). Death occurred in 9.9% of patients in the restrictive strategy and 8.3% of patients in the liberal strategy (relative risk, 1.19 [95% CI, 0.94-1.49]), and cardiac death occurred in 5.5% of patients in the restrictive strategy and 3.2% of patients in the liberal strategy (relative risk, 1.74 [95% CI, 1.26-2.40]). Although the MINT trial did not demonstrate a statistically significant reduction in its primary endpoint, the results suggest that a liberal blood transfusion strategy targeting a hemoglobin level around 10 g/dL may provide short-term clinical benefit over a restrictive transfusion strategy targeting a hemoglobin level above 7 g/dL or 8 g/dL in patients with AMI and anemia.

10.3. Telemetry and Length of Stay

Recommendation for Telemetry and Length of Stay		
COR	**LOE**	**Recommendation**
1	**C-LD**	1. In patients with ACS, telemetry monitoring is recommended to reduce cardiovascular events with duration determined by cardiac risk.[1,2]

Synopsis

Advances in vascular access methods, coronary revascularization, and concomitant medical therapies have contributed to shortening length of stay and further facilitated changes in discharge patterns after PCI in the setting of ACS. There remains limited evidence

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regarding the optimal length of stay after MI. Patients with STEMI represent a higher risk cohort who may require longer length of stay. Available data suggest that an early discharge strategy of <3 days from admission is not associated with increased mortality for low-risk patients after STEMI who have undergone PCI.[3–8] The Zwolle score has been recommended as a clinical tool to help identify patients after PPCI in STEMI at low risk of death (low-risk patients, score ≤3) who can potentially be discharged earlier from the hospital (48 to 72 hours). Predictors of mortality in the Zwolle score include age, Killip class, postprocedural TIMI Flow Grade, 3-vessel disease, anterior infarction, and ischemic time.[3] Optimal length of stay in the setting of NSTE-ACS has been less rigorously studied. Small retrospective studies have suggested safety of very early or same-day discharge after PCI for patients with ACS, with most (71%) of same-day discharge being troponin-negative.[9] Patients being considered for early discharge should be clinically stable without evidence of ongoing ischemia, acute kidney injury, LV dysfunction, HF, and procedural complications and with adequate postdischarge support.[8] Hospitals and care providers should ensure that patients have access to postdischarge prescription medications and adequate follow-up.

Recommendation-Specific Supportive Text

1. The number of studies addressing telemetry duration are few and the focus has been on arrhythmia monitoring, not continuous ST-segment monitoring. Continuous ST-segment monitoring can be considered for higher-risk patients, including those with suspected ischemia who are not yet revascularized.[1,10–14] Patients with ACS who are at low risk for cardiac arrhythmias require rhythm monitoring for ≤24 hours or until coronary revascularization (whichever comes first) in a telemetry unit, while individuals at intermediate to high risk for cardiac arrhythmia may require rhythm monitoring for >24 hours in a telemetry unit or in an intermediate care unit, depending on the clinical presentation, degree of revascularization, and early postrevascularization course with input from the treating cardiologist.[10,12–14]

10.4. Noninvasive Diagnostic Testing Prior to Hospital Discharge

Recommendation for Noninvasive Diagnostic Testing Prior to Hospital Discharge		
COR	**LOE**	**Recommendation**
1	**C-LD**	1. In patients with ACS, an assessment of LVEF is recommended prior to hospital discharge to guide therapy and for risk stratification.[1–3]

Synopsis

In patients with ACS, LV function should be routinely evaluated in patients prior to hospital discharge to help guide therapy and for risk stratification.[1–3] Transthoracic echocardiography is generally the preferred modality because it is noninvasive and can provide a comprehensive assessment of ventricular and valvular function, as well as possibly detect LV thrombus or mechanical complications. Transthoracic echocardiography is therefore strongly preferred for all patients hospitalized with STEMI because complications may be more likely to be present. In patients where transthoracic echocardiography is nondiagnostic, cardiac magnetic resonance imaging is a reasonable alternative in clinically stable patients. Alternatively, LV function and some mechanical complications can be assessed invasively with left ventriculography in the cardiac catheterization laboratory, but other data regarding valvular function and wall motion are best evaluated with noninvasive methods like transthoracic echocardiography or cardiac magnetic resonance imaging. LV function may also be estimated noninvasively by myocardial perfusion imaging testing, but this will also provide incomplete information regarding the presence or absence of other complications of MI. For patients in whom LV function is found to be reduced, a repeat echocardiogram should be performed in 6 to 12 weeks to further guide treatment decisions and for consideration of need for an ICD.[4,5]

Recommendation-Specific Supportive Text

1. LV function should be routinely evaluated in patients with ACS prior to hospital discharge because LVEF guides therapeutic interventions and facilitates risk stratification. The diagnosis of LV dysfunction is important because it may trigger consideration for the initiation or optimization of guideline-directed therapeutic interventions for patients with HF or depressed LV function. It also helps identify patients with reduced LVEF who may require consideration for future primary prevention implantation of an ICD. Besides LVEF, transthoracic echocardiography facilitates the assessment of regional wall motion abnormalities, valvular function, mechanical complications,[4] and LV thrombus.[5] In cases in which LV function cannot be adequately assessed despite the use of contrast echocardiography, cardiac magnetic resonance is the preferred imaging modality for clinically stable patients.[6–9]

10.5. Discharge Planning

10.5.1. Patient Education

Synopsis

Patient education is universally valued and aims to deliver information from clinicians to patients to improve

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health behavior and long-term health-related outcomes. Clinicians are well positioned to engage in meaningful dialogue with patients who have experienced an ACS event about secondary prevention and building self-care skills to manage their condition (Table 20). Recovery represents a teachable moment to provide structured education, including priming the patient to attend cardiac rehabilitation (CR). Systematic reviews of educational interventions targeting secondary prevention in patients with coronary heart disease, many of whom have ACS, have demonstrated effectiveness in improving disease-related knowledge, healthy behaviors (eg, smoking cessation, physical activity, healthy dietary behavior), and medication adherence.[1–3] The magnitude of the effect on each of these outcomes varies by study. Beyond improved knowledge and behavior change, the impact of individualized education for patients with ACS on morbidity and mortality is less clear. A shortcoming of published educational intervention studies to date is that the interventions are markedly heterogeneous but vary in intensity, duration, delivery mode, resources needed, and outcomes measured. Currently, insufficient comparative data are available to guide clinicians about which specific educational interventions are best. However, evidence supports the use of individualized goal setting that demonstrates respect for the patient and their circumstances, structured content that is culturally appropriate, and clearly defined outcomes.[4] Table 20 lists the components that should be discussed with ACS patients at the time of hospital discharge.

10.5.2. Postdischarge Follow-Up and Systems of Care Coordination

Synopsis

Transition from the hospital to home is a critical period for patients with ACS because approximately 1 in 5 patients are readmitted within 30 days of discharge.[1–6] Women, individuals from traditionally underrepresented racial and ethnic groups, and patients who require ICU services during their index hospitalization are particularly at risk for readmission.[3] Quality improvement programs such as the Hospital to Home Initiative[7] or the AMI Toolkit[8] provide resources to assist clinicians decrease readmission rates and improve medication and CR adherence through increased provider communication and care coordination. Transitional care interventions that leverage different types of support (eg, hospital-initiated support, patient and family education delivered before and after discharge, or community-based or chronic disease management models of care) are examples of ways to reduce risk of readmission.[9] Hospital-initiated support interventions are associated with reduced mortality rates at 3 months and 1 year as well as a reduction in 30-day readmission rates among patients with AMI.[9,10] Multicomponent integrated care (≥2 quality improvement strategies targeting different domains of the health care system, health care professionals, or patients) as compared with usual care has been associated with reduction of all-cause death, cardiovascular mortality, and all-cause hospitalization.[11] Emerging digital health interventions hold promise to improve the transition from hospital to home. For additional recommendations on nutrition, physical activity, smoking cessation, and alcohol and substance use, refer to the "2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline for Management of Patients With Chronic Coronary Disease."[12] Table 21 summarizes the recommended guidance for hospital discharge.

Table 20. Essential Components of Patient Education

Reason for hospitalization (explain reason for admission, diagnostic tests, procedural results)
Tailored discussion of lifestyle modifications (AHA's Life's Essential 8)[5]
Medications (written and verbal instructions including purpose, dose, frequency, potential adverse effects of each medication; refill instructions; changes to prehospital regimen; importance of adherence)
Symptom management (what to monitor for and actions to take should symptoms recur, including whom to call)
Returning to daily routine (when to resume physical activity, sexual activity, work, and travel)
Psychosocial considerations (open dialogue about symptoms of depression and anxiety)
Follow-up care (future appointments with cardiology, CR, additional testing postdischarge)

AHA indicates American Heart Association; and CR, cardiac rehabilitation.

10.5.3. Cardiac Rehabilitation

Recommendations for CR Referenced studies that support recommendations are summarized in the Evidence Table.		
COR	**LOE**	**Recommendations**
1	A	1. Patients with ACS should be referred to an outpatient CR program prior to hospital discharge to reduce death, MI, hospital readmissions, and improve functional status and QOL.[1–4]
2a	B-R	2. In patients with ACS, a home-based CR program is a reasonable alternative to a center-based CR program to improve functional status and QOL.[5–9]

Synopsis

CR is a multifaceted and comprehensive outpatient intervention that is considered the standard of care for secondary prevention of CVD. The primary goals of CR are modifying CVD risk factors and improving patient functional capacity and QOL with the goal of reducing subsequent morbidity and mortality. Through a combination of monitored exercise training, health and nutrition education, psychological support, and personalized patient assessment, including medication optimization (Figure 10), CR has been shown to lower the risk of cardiovascular and all-cause death, reduce hospital readmissions, and to be cost-effective.[10,11] Despite its proven benefits, CR is underutilized and referral rates to CR are low, especially for wom-

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Table 21. Guidance for ACS Discharge: Best Practices

Communication	Patient centered, verbally and in writing in patient/caregiver preferred language Shared decision-making regarding assessment of goals and preferences should be discussed with patient/caregiver
Clinical assessment	Address comorbidities and risk factors for recurrent events Assess for presence of ongoing ischemic symptoms, using standardized instrument ideally embedded into EHR Assess risk for bleeding related to medications or procedural site Assess need for additional testing (eg, repeat echocardiogram, staged PCI) Assess whether vaccinations are current (eg, influenza) Perform medication reconciliation, including a prescription for sublingual nitroglycerin, unless contraindicated
Patient/caregiver assessment	Assess capacity for patient/caregiver for self-care (eg, secondary prevention, symptom monitoring, following plan of care, lifestyle changes, contact information for continuing care team) Provide verbal and written educational information related to self-care Use teach-back method to confirm understanding of self-care Use teach-back method for patient/caregiver understanding of medication adherence and treatment regimen
Referrals	Confirm referral to CR Provide educational materials related to CR including contact information
Social determinants of health	Assess and address barriers to obtaining and taking prescribed medications, to include referral to pharmacy assistance programs or social worker as appropriate Assess and address barriers to attending CR, including viability of home-based or hybrid CR

ACS indicates acute coronary syndromes; CR, cardiac rehabilitation; EHR, electronic health record; and PCI, percutaneous coronary intervention.

en and members of traditionally underrepresented groups.[8] Factors that contribute to this overall low enrollment rate include a poor utilization of a centralized method for referral via the electronic health record, inadequate communication between treatment teams, and perceived inconvenience as well as associated costs for the patient.[8] To increase the utilization of CR, patients should be referred to CR during hospitalization for ACS and prior to discharge.[12] To improve access for patients who live in rural locations and in areas with no center-based CR, home-based CR options should be considered. These home-based CR programs have similar shorter-term safety and clinical outcomes (eg, improvements in exercise capacity, QOL, blood pressure, cholesterol) as center-based CR.[13–15] More intensive CR programs have been developed with a goal of expanding the benefits of traditional CR programs through additional exercise and education sessions, as well as placing a greater focus on diet and lifestyle factors.[16–18] Although improved outcomes have been described with an intensive program,[16,19] the studies are observational in nature. Both traditional and intensive CR programs remain underutilized, so the primary emphasis should be on enrollment and adherence to any CR program.[20]

Recommendation-Specific Supportive Text

1. Exercise-based CR programs are associated with improved survival and reduced risk of reinfarction in patients after AMI.[1–4] CR can be enhanced as a component of a multifactorial rehabilitation program with risk factor education and counseling. Patients with ACS who participate in CR have significantly better outcomes compared with those who do not.[1,21,22] In a meta-analysis of 85 RCTs of exercise-based CR in patients with coronary heart disease, the intervention reduced risk of MI, reduced all-cause hospitalization, reduced health care costs, and improved health-related QOL outcomes over 12 months of follow-up.[1] Longer follow-up suggested reductions in cardiovascular mortality.[1,4] CR is particularly beneficial in older patients with CAD, a group that is at a higher risk of losing independence and functioning.[23–26]
2. To overcome challenges that have prevented greater patient participation, new strategies and innovative models that utilize digital health tools are emerging to meet the evolving needs of CR patients. CR programs have traditionally been delivered via center-based CR. These programs require patients to be physically present at a facility located in a hospital or outpatient center, which limits access for many patients, especially women and some racial and ethnic groups.[9,27,28] A review of 23 RCTs of home- and center-based CR found that these programs tend to implement the same core components.[13] These include patient assessment of current medical history, exercise training, dietary counseling, risk factor management (eg, smoking, lipids, blood pressure, weight, diabetes), and psychological intervention. Comparison of studies in home- and center-based CR indicate a similar improvement in QOL and no statistically significant difference in the all-cause mortality rate up to 12 months after the intervention.[5,6] However, more RCTs are needed with home-based CR in patients with ACS because of an evidence gap (especially in high-risk patients) in assessing the safety of home-based CR in patients at high risk for recurrent ischemic events, as well the impact of a home-based rehabilitation strategy on clinical outcomes such as cardiovascular death, recurrent MI, and rehospitalization.[29] Advances in technology and remote monitoring may help to improve the efficacy and safety of this approach. Hybrid models that combine elements of both center- and home-based programs may also offer benefits.

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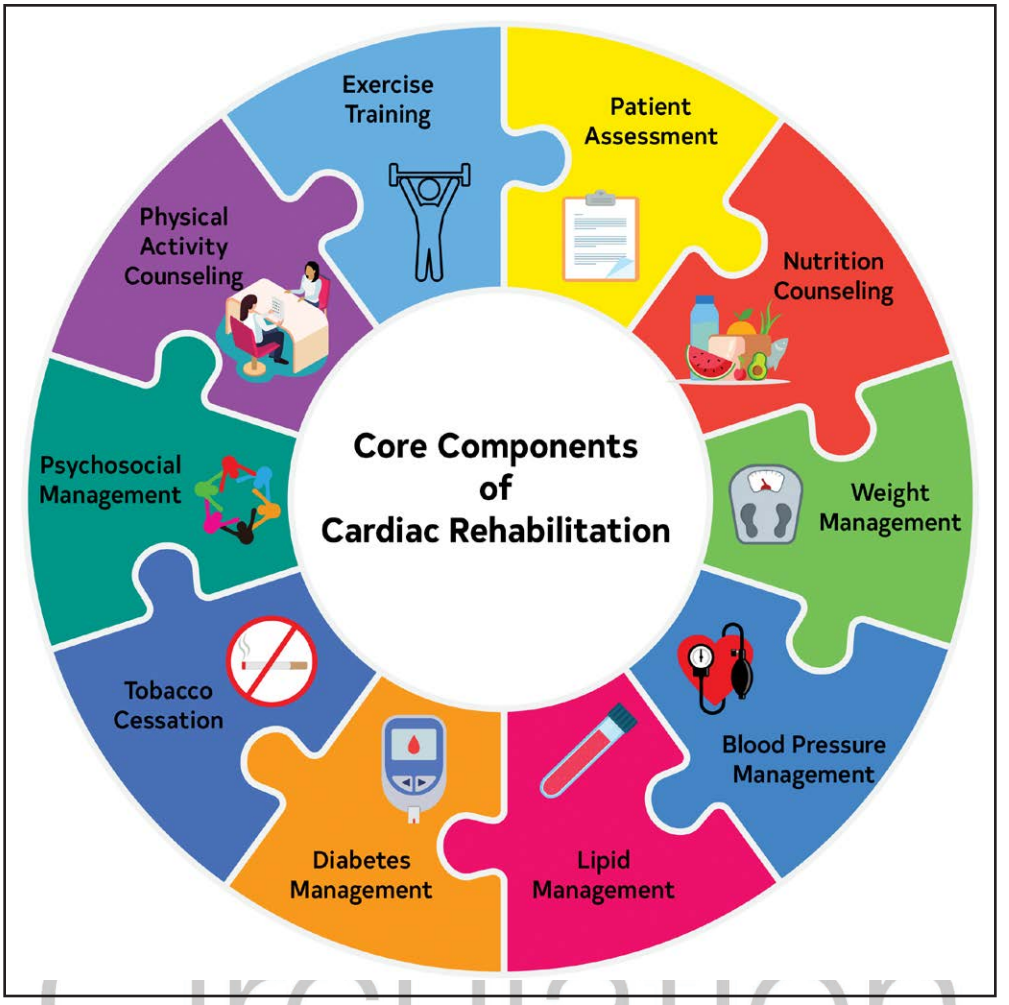

Figure 10. Core Components of Cardiac Rehabilitation.
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11. DISCHARGE: LONG-TERM MANAGEMENT AND SECONDARY PREVENTION

11.1. DAPT Strategies in the First 12 Months Postdischarge

Recommendations for DAPT Strategies in the First 12 Months Postdischarge Referenced studies that support recommendations are summarized in the Evidence Table.		
COR	**LOE**	**Recommendations**
Default Duration of DAPT		
1	A	1. In patients with ACS who are not at high bleeding risk, DAPT with aspirin and an oral P2Y12 inhibitor should be administered for at least 1 year to reduce MACE.[1–6]

Recommendations for DAPT Strategies in the First 12 Months Postdischarge (Continued)		
COR	**LOE**	**Recommendations**
Bleeding Reduction Strategies		
1	A	2. In patients with ACS who have tolerated DAPT with ticagrelor, transition to ticagrelor monotherapy ≥1 month post PCI is useful to reduce bleeding risk.[7–11]
1	A	3. In patients at high risk of gastrointestinal bleeding, a proton pump inhibitor (PPI) is recommended in combination with DAPT, oral anticoagulants, or both to reduce risk of bleeding.[12–15]
2b	B-R	4. In patients with ACS undergoing PCI, de-escalation of DAPT (switching from ticagrelor or prasugrel to clopidogrel) after 1 month may be reasonable to reduce bleeding risk.[16–20]
2b	B-R	5. In patients with ACS undergoing PCI who are at high bleeding risk, transition to single antiplatelet therapy (aspirin or P2Y12 inhibitor) after 1 month may be reasonable to reduce bleeding risk.[21]

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Synopsis

The addition of an oral P2Y12 inhibitor to aspirin (DAPT) reduces the risk of early and late thrombotic events among patients with ACS regardless of whether they are managed with an invasive strategy.[1–3] Notwithstanding these salutary benefits, prolonged exposure to DAPT results in excess bleeding that may lead to DAPT interruption,[22] which in turn may increase the risk of recurrent ischemic events.[23] Identifying individuals most likely to realize a net clinical benefit or harm from prolonged DAPT has emerged as an important clinical priority. Several tools have been developed that predict the risk of ischemic and/or bleeding events and may be useful when considering how best to personalize care for an individual patient.[24–27] Moreover, alternative antiplatelet strategies have been compared with conventional DAPT with the intent to reduce bleeding while maintaining ischemic efficacy. Growing evidence suggests that a strategy of aspirin discontinuation with ticagrelor monotherapy reduces bleeding.[7–11] Although clopidogrel monotherapy has been studied,[28,29] interpatient variability in pharmacodynamic response to clopidogrel is substantial[30] and may increase thrombotic risk in certain individuals. To that end, a strategy of clopidogrel monotherapy may increase risk of MACE in patients after ACS when compared with more prolonged DAPT.[29] Additional approaches include aspirin monotherapy[31,32] or a strategy of "de-escalation" (ie, switching from ticagrelor or prasugrel to clopidogrel),[16–20] although the safety of these strategies in terms of their effects on risk of MACE is less firmly established. Efficacy and safety of shorter DAPT strategies have not been rigorously studied in patients not undergoing PCI. Figure 11 summarizes the guideline recommendations for DAPT management in patients with ACS during the first 12 months post discharge.

Recommendation-Specific Supportive Text

1. Patients with ACS are characterized by a sustained prothrombotic state,[33] thus highlighting the need for continued antithrombotic therapy beyond the index presentation. The double-blind placebo-controlled CURE (Clopidogrel in Unstable Angina to Prevent Recurrent Events) trial (n=12 562) demonstrated that DAPT with clopidogrel yields a consistent reduction in both early and late composite ischemic events as compared with aspirin alone among patients with NSTE-ACS who were primarily managed medically.[3,34] The treatment effect was consistent among those treated with or without revascularization.[4] Subsequent studies showed that DAPT with prasugrel or ticagrelor administered for 1 year provides incremental reductions in ischemic events, albeit with excess bleeding, as compared with clopidogrel.[1,2] Although concordant benefits were also observed among trial participants requiring surgical revascularization, the safety and efficacy of DAPT should be considered in the context of CABG as a postrandomization event and the high proportion of patients who did not resume study drug after surgery.[4–6] An important consideration in extending the results of clinical trials that established the benefits of DAPT to contemporary cohorts is that patients at elevated risk for bleeding were typically excluded in early studies. Therefore, the default strategy for a minimum DAPT duration of 1 year is most applicable to those patients without high bleeding risk presenting with ACS. Moreover, the choice of P2Y12 inhibitor may vary in relation to treatment approach, as described in Section 4.3.2, "Oral P2Y12 Inhibitors During Hospitalization." In select patients who have tolerated DAPT, it may be reasonable to extend treatment beyond 1 year after considering risks for long-term bleeding and thrombosis.[35–37]
2. Results from several randomized trials have consistently shown that aspirin withdrawal followed by ticagrelor monotherapy after 1 to 3 months of ticagrelor-based DAPT results in less bleeding without clear excess in MACE, as compared with continued DAPT among patients with ACS undergoing PCI.[7–11] Although studies examining this strategy were characterized by relatively low rates of ischemic events, study-level[38] and individual patient data pooled analyses[39–41] have yielded similar results. Although data with clopidogrel have been mixed, concerns have been raised that a strategy of clopidogrel monotherapy started 1 to 2 months after PCI may increase risk of MACE in patients with ACS when compared with longer DAPT.[29] It remains unknown whether this may be explained by excess thrombotic risk in patients displaying inadequate platelet inhibition to clopidogrel, observed in 30% to 40% of patients after PCI.[30,42] Results from a randomized trial showed that a strategy of P2Y12 inhibitor discontinuation followed by aspirin alone after 6 months of DAPT resulted in excess thrombotic risk among patients with ACS undergoing PCI (n=2712; 38% STEMI), albeit with less bleeding.[32] Similar findings were observed with earlier P2Y12 inhibitor discontinuation 3 months after PCI.[31,43] Although the on-treatment pharmacodynamic effects of ticagrelor and prasugrel are similar, the safety of a strategy of prasugrel monotherapy has not been established in patients ≥1 month post ACS; low-dose prasugrel monotherapy (3.75 mg daily) in Japanese patients very early after PCI with ACS or at high bleeding risk may increase 30-day MACE compared with DAPT.[44]
3. PPIs reduce the risk of gastrointestinal bleeding among patients receiving aspirin,[14] DAPT,[13] or an

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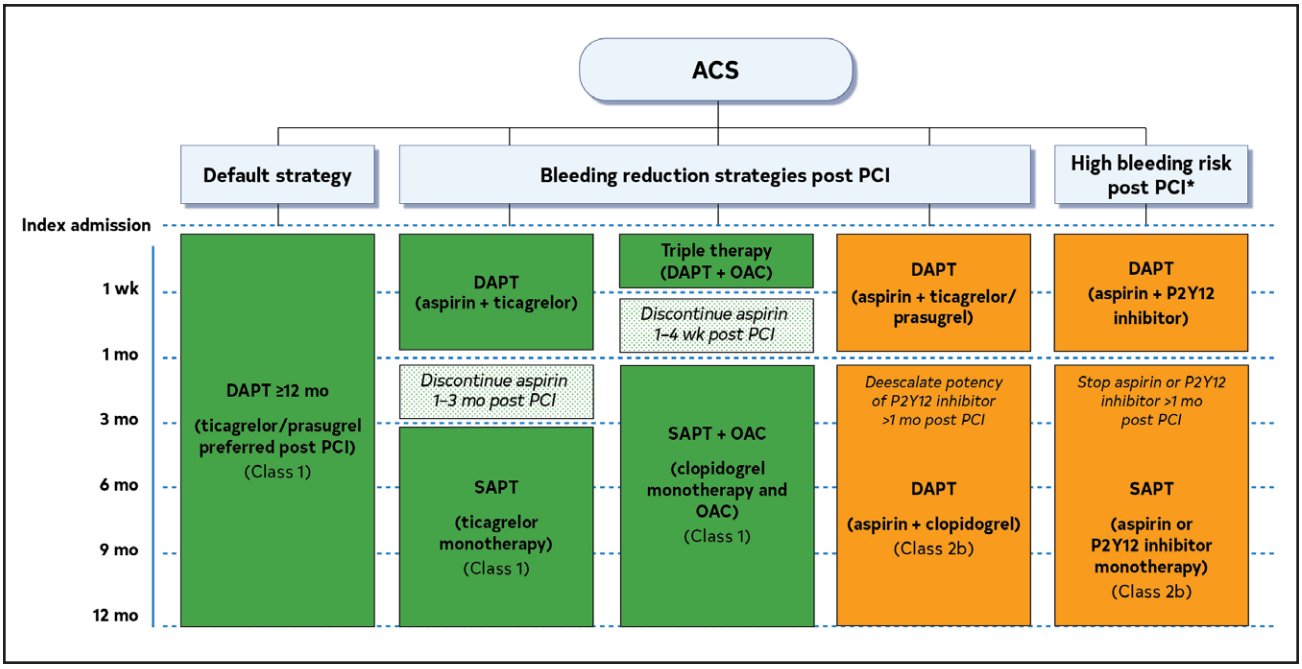

Figure 11. DAPT Strategies in the First 12 Months Postdischarge.
Colors correspond to Class of Recommendation in Table 2. *High bleeding risk discussed in Section 11.1, "Recommendation-Specific Supportive Text" item 5, and outlined in Table 22. ACS indicates acute coronary syndromes; DAPT, dual antiplatelet therapy; OAC, oral anticoagulant; PCI, percutaneous coronary intervention; and SAPT, single antiplatelet therapy.

oral anticoagulant.[12,15] Because the conversion of clopidogrel to its active metabolite and the metabolism of certain PPIs depend on some common hepatic enzymes (eg, CYP2C19), the potential for a drug-drug interaction exists when both agents are coadministered. The results of several ex vivo studies found that clopidogrel-induced platelet inhibition is attenuated with use of certain PPIs, a pharmacodynamic effect that is most pronounced with omeprazole.[45,46] Nonetheless, results from a double-blind, placebo-controlled randomized trial showed no significant differences in ischemic events between omeprazole versus placebo among patients treated with clopidogrel, but PPI use markedly decreased the risk of gastrointestinal bleeding.[13] Moreover, post hoc analyses from several randomized trials have shown that ischemic risk is not increased when a clinically indicated PPI is used with clopidogrel.[47,48] Importantly, the antiplatelet effects and clinical efficacy of ticagrelor and prasugrel are not appreciably modified with concomitant PPI use.[48–50] Therefore, it is recommended to administer a PPI in patients with ACS at elevated bleeding risk treated with DAPT or oral anticoagulant.

4. De-escalation implies modulating DAPT intensity by switching from ticagrelor or prasugrel to clopidogrel.[51] De-escalation can be guided by the results of platelet function assays that quantify the degree of platelet inhibition among patients treated with clopidogrel. Patients with adequate response may continue to receive clopidogrel, whereas nonresponders are switched to a more potent P2Y12 inhibitor. Clopidogrel responsiveness may also be inferred with use of genotyping assays that identify polymorphisms in genes involved in clopidogrel metabolism.[52] Clinical trials examining guided de-escalation after PCI have either shown a lack of benefit,[16] noninferiority,[20] or reductions in minor bleeding[17] versus conventional DAPT. By contrast, unguided de-escalation is performed without antecedent knowledge of platelet responsiveness. Randomized trials have suggested that unguided de-escalation 1 month after PCI reduces bleeding without incurring ischemic risk as compared with longer term prasugrel- or ticagrelor-based DAPT.[18,19] Pooled analyses have shown that de-escalation (guided or unguided) yields comparable efficacy to DAPT with respect to ischemic events while reducing bleeding.[53,54] However, trials of ticagrelor and prasugrel have suggested that the benefit of more potent P2Y12 inhibitor therapy extends beyond the early phase post ACS, but with increased bleeding.[1,2,55]
5. In the MASTER DAPT (Management of High Bleeding Risk Patients Post Bioresorbable Polymer Coated Stent Implantation With an Abbreviated Versus Standard DAPT Regimen) trial, patients at high risk of bleeding who had completed a 4-week course of DAPT after successful PCI with drug-eluting stents were randomly allocated to single antiplatelet therapy or more prolonged DAPT (≥2

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Table 22. Academic Research Consortium High Bleeding Risk Criteria After PCI

Major Criteria[26]	Minor Criteria
	Age ≥75 y
Anticipated use of long-term oral anticoagulation (Section 11.1.1, "Antiplatelet Therapy in Patients on Anticoagulation Postdischarge")	
Severe or end-stage CKD (eGFR <30 mL/min)	Moderate CKD (eGFR 30-59 mL/min)
Hemoglobin level <11 g/dL	Hemoglobin level 11-12.9 g/dL for men and 11-11.9 g/dL for women
Spontaneous bleeding requiring hospitalization or transfusion in the past 6 mo or at any time, if recurrent	Spontaneous bleeding requiring hospitalization or transfusion within the past 12 mo not meeting the major criterion
Moderate or severe baseline thrombocytopenia (platelet count <100×10^9/L)	
Chronic bleeding diathesis	
Liver cirrhosis with portal hypertension	
	Long-term use of oral NSAIDs or steroids
Active malignancy (excluding nonmelanoma skin cancer) within the past 12 mo	
Previous spontaneous ICH (at any time) Previous traumatic ICH within the past 12 mo Presence of a brain arteriovenous malformation Moderate or severe ischemic stroke within the past 6 mo	Any ischemic stroke at any time not meeting the major criterion
Nondeferrable major surgery on DAPT	
Recent major surgery or major trauma within 30 d before PCI	

The presence of at least 1 major or 2 minor criteria helps to identify those at increased risk of bleeding. Modified with permission from Urban et al.[26] Copyright 2019 American Heart Association, Inc.

CKD indicates chronic kidney disease; DAPT, dual antiplatelet therapy; eGFR, estimated glomerular filtration rate; NSAID, nonsteroidal anti-inflammatory drugs; ICH, intracranial hemorrhage; and PCI, percutaneous coronary intervention.

additional months).[21] In the absence of oral anticoagulant use, the choice of discontinuing aspirin or P2Y12 inhibitor and the choice of P2Y12 inhibitor was at the discretion of the treating physician. An oral anticoagulant was used in 36.4% of patients, and clopidogrel monotherapy was selected in 53.9% of patients randomized to abbreviated DAPT. Compared with standard therapy, an abbreviated antiplatelet strategy demonstrated noninferiority with respect to composite ischemic events and superiority regarding clinically relevant bleeding over 1 year. Among patients with ACS (n=1780; 30% STEMI) allocated to an abbreviated strategy, clinicians selected a potent P2Y12 inhibitor with ticagrelor use in approximately 25% of patients.[56] Results in the ACS cohort were qualitatively consistent with the overall trial results with respect to both ischemic and bleeding outcomes. Although the trial demonstrated noninferiority for abbreviated DAPT with respect to MACE in patients at high bleeding risk, it was underpowered to determine the relative safety of discontinuing aspirin versus P2Y12 inhibitor. Multiple studies have identified clinical and laboratory predictors of bleeding and/or ischemic risk.[24–27] The Academic Research Consortium determined 20 correlates of bleeding and proposed a consensus-based definition of high bleeding risk as the presence of having at least 1 major or 2 minor criteria at time of PCI (Table 22).[26]

11.1.1. Antiplatelet Therapy in Patients on Anticoagulation Postdischarge

Recommendation for Antiplatelet Therapy in Patients on Anticoagulation Postdischarge Referenced studies that support recommendation are summarized in the Evidence Table.		
COR	**LOE**	**Recommendation**
1	B-R	1. In patients with ACS who require oral anticoagulant therapy, aspirin should be discontinued after 1 to 4 weeks of triple antithrombotic therapy, with continued use of a P2Y12 inhibitor (preferably clopidogrel) and an oral anticoagulant to reduce bleeding risk.*[1–5]

*Modified from the "2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization."[6]

Synopsis

Patients after ACS may frequently have indications for anticoagulant therapy, including AF, venous thromboembolism, and prosthetic heart valves. Bleeding risks are increased in the setting of triple therapy with the combination of aspirin, P2Y12 inhibitor, and anticoagulant. Therefore, the benefits of these therapies must be weighed against the risk of bleeding. A growing number of studies have demonstrated the overall safety of a strategy of aspirin discontinuation 1 to 4 weeks after ACS or PCI in patients who require anticoagulation after ACS.[1–5] For most patients, a DOAC will be preferred over a vitamin K antagonist due to their favorable efficacy and safety profile.[7] Trials of more potent P2Y12 inhibitors

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(ie, prasugrel and ticagrelor) excluded patients requiring long-term anticoagulation; therefore, clopidogrel is generally favored as the P2Y12 inhibitor in this setting for most patients. The decision whether to continue anticoagulant with or without antiplatelet therapy >12 months after ACS is addressed in the "2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline for the Management of Patients with Chronic Coronary Disease."[8]

Recommendation-Specific Supportive Text

1. Several RCTs have demonstrated that the discontinuation of aspirin 1 to 4 weeks after PCI reduces the risk of bleeding in patients with AF with an indication for DAPT and an oral anticoagulant.[1–5] Although individual studies were not powered for ischemic endpoints, meta-analyses across randomized trials suggest no difference in mortality, stroke, and overall MACE when aspirin is discontinued for patients on an oral anticoagulant, albeit with a marginal apparent increase in MI and stent thrombosis.[9–14] An analysis of stent thrombosis rates suggested that 80% of events occurred within 30 days of PCI, with stent thrombosis events numerically less frequent in those receiving aspirin (randomization was approximately 1 week after PCI) compared with placebo in the AUGUSTUS (Antithrombotic Therapy After Acute Coronary Syndrome or PCI in Atrial Fibrillation) trial.[15,16] Therefore, in patients with a high risk of stent thrombosis, aspirin for up to 30 days after PCI could be considered. P2Y12 inhibitor therapy should be continued for at least 12 months after PCI following aspirin discontinuation but could be discontinued earlier in those with multiple risk factors for bleeding.[17,18]

11.2. Reassessment of Lipid Levels Postdischarge

Recommendation for Reassessment of Lipid Levels Postdischarge		
COR	**LOE**	**Recommendation**
1	C-LD	1. In patients after ACS, a fasting lipid panel is recommended 4 to 8 weeks after initiation or dose adjustment of lipid-lowering therapy to assess response or adherence to therapy.*[1,2]

*Modified from the "2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol."[3]

Synopsis

Aggressive LDL-C lowering is an important component of secondary CVD prevention. For every 1.0-mmol/L (~39 mg/dL) reduction of LDL-C, an approximate 22% relative reduction in cardiovascular events is observed over a period of 4 to 5 years.[2] Despite the growing number of lipid-lowering therapies currently available, many patients with ACS do not achieve target LDL-C levels.[4,5] The reasons are varied but include underprescribing by providers, cost or insufficient coverage by medical insurance companies, and intolerance to therapies. Many patients are also unwilling or unable to readily fill prescriptions at pharmacies or patients self-discontinue therapy early. Providers are not always aware of the barriers that patients may be experiencing; therefore, a conversation between clinician and patient is important to help improve adherence. If adverse effects are experienced, consideration should be given to subsequent rechallenge at each visit or changing to a different type of statin or class of lipid-lowering therapy. Statin intolerance requires exposure to at least 2 different statins with 1 prescribed at the lowest available dose. Because risk of MACE is elevated in the early months after ACS, early follow-up visits are important for making appropriate changes to lipid-lowering therapy to help achieve desired LDL-C targets (Section 4.5, "Lipid Management"). Importantly, lipid-lowering therapies should not be downtitrated in response to very low LDL-C concentrations, because current evidence supports that those with very low LDL-C concentrations are at lowest risk of MACE without any clear safety concern.[6–9]

Recommendation-Specific Supportive Text

1. Use of high-potency statin therapy has been shown to reduce MACE with the benefit appearing early after ACS and persisting with time.[10] To date, evidence suggests the benefit of lowering LDL-C concentrations may be irrespective of whether it is achieved through high-potency statins or other lipid-lowering therapies; however, the largest body of evidence exists with statin therapies. As such, early intensification of lipid-lowering therapy after ACS is justified. In clinical practice, statin-eligible patients remain undertreated or untreated.[1,11] Early and frequent follow-up, including lipid testing, is associated with improved adherence to lipid-lowering therapies.[1] In the PALM (Provider Assessment of Lipid Management) registry, less than one-half of adults were on the statin intensity recommended by the guidelines.[12] In a study of US veterans with a history of ACS or coronary revascularization, less than one-half of patients received intensification of lipid-lowering therapy (41.9% at 3 months versus 47.3% at 1-year postdischarge).[5] High patient copays and poor coverage of newer lipid-lowering therapies by some prescription plans are factors contributing to suboptimal LDL target attainment. To that end, out-of-pocket costs should be verified and discussed with patients before they fill a prescription for a new lipid-lowering therapy. Education about the importance of lipid-lowering therapies should be discussed with patients at

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visits to allow them the opportunity to ask questions and review potential barriers. For the management of lipid-lowering therapy initiated prior to discharge and continued after hospital discharge, refer to Section 4.5, "Lipid Management."

11.3. SGLT-2 Inhibitors and GLP-1 Receptor Agonists

Synopsis

The cardiovascular benefits of both sodium glucose cotransporter-2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists are well documented in stable patients with ASCVD and type 2 diabetes,[1–6] as well as in patients with HF regardless of diabetes status.[7–11] GLP-1 receptor agonists may lead to weight loss in many patients, and semaglutide has been shown to reduce the risk of MACE in overweight or obese patients with stable ASCVD but has not been studied early after ACS.[12] SGLT-2 inhibitors may increase the risk of urinary tract infection, genital mycotic infection, hypovolemia, and acute kidney injury (while offering longer term renal benefit in patients with diabetes). Due to a higher risk of diabetic and euglycemic ketoacidosis in the perioperative period, canagliflozin, dapagliflozin, and empagliflozin should be stopped ≥3 days and ertugliflozin ≥4 days prior to scheduled surgery, including CABG.[13–15]

The efficacy and safety of SGLT-2 inhibitors have now been studied in 2 large trials of patients after MI. In patients without diabetes or HF, dapagliflozin was not shown to reduce the risk of cardiovascular death or HF hospitalization in patients with AMI and impaired LV systolic function.[16] Similarly, empagliflozin did not significantly reduce all-cause death or first HF hospitalization in patients without prior HF who were hospitalized with AMI and found to have impaired LV systolic function with or without signs of congestion. However, empagliflozin did reduce HF hospitalizations in this population.[17] No new safety concerns were identified. Therefore, use of an SGLT-2 inhibitor does not need to be deferred in patients with an indication for its use at hospital discharge.

11.4. Use of Chronic Colchicine

Recommendation for Use of Chronic Colchicine Referenced studies that support recommendation are summarized in the Evidence Table.		
COR	**LOE**	**Recommendation**
2b	B-R	1. In patients after ACS, low-dose colchicine may be reasonable to reduce risk of MACE.[1–5]

Synopsis

Colchicine is a botanical-derived anti-inflammatory agent that has been used for millennia in the treatment of gout. Colchicine reduces neutrophil adhesion to endothelial cells and platelets and has been shown to reduce high-sensitivity C-reactive protein concentration and low-attenuation plaque volume in patients already on aspirin and statin therapy.[6–9] Colchicine is associated with a lower risk of MI in patients with gout, as well as in patients with CAD, including those with prior MI.[1,4,5,10,11] Although gastrointestinal events were historically reported at a higher rate in patients on colchicine, this rate does not differ from placebo at the lower once daily dosing.[5] A meta-analysis of the studies examining colchicine in patients with CAD reported no difference in all-cause death with colchicine versus placebo, but a nonsignificant trend was observed toward an increased risk of noncardiovascular death that requires further study.[5] To date, no potential pathogeneses of the noncardiovascular deaths have been consistently shown to explain the numerical differences in noncardiovascular death.[5]

Recommendation-Specific Supportive Text

1. COLCOT (Colchicine Cardiovascular Outcomes Trial) randomized patients ≤30 days (median, 14 days) after MI to low-dose colchicine versus placebo.[2] Colchicine reduced the primary outcome of cardiovascular death, resuscitated cardiac arrest, MI, stroke, or urgent coronary revascularization by 32% (median follow-up, 22.6 months). Although directional consistency was seen across individual components, this benefit was driven by a reduction in hospitalizations for angina requiring revascularization and stroke. The smaller COPS (Colchicine in Patients With ACS) study randomized patients during their index hospitalization of ACS to colchicine versus placebo.[3] The primary endpoint of all-cause death, ACS, unplanned ischemia-driven urgent revascularization, and noncardioembolic ischemic stroke was numerically, but not significantly, lower for patients on colchicine (P=0.09). Although deaths were infrequent, more deaths occurred for patients on colchicine than on placebo (8 versus 1; P=0.017) due to more noncardiovascular deaths. In a post hoc analysis, the composite outcome of cardiovascular death, ACS, stroke, or urgent revascularization was lower for colchicine than placebo. The LoDoCo2 (Low-Dose Colchicine-2) trial enrolled patients with stable (>6 months) coronary disease, demonstrating a reduction in the composite of cardiovascular death, MI, ischemic stroke, or ischemia-driven coronary revascularization with colchicine (median follow-up, 28.6 months); findings were consistent in the 84% of patients with prior ACS.[4,12] Pooled data from these large trials confirmed a reduction in the incidence of MACE with colchicine versus placebo.[5] Colchicine should not be administered in patients with blood

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dyscrasias, renal failure (creatinine clearance <15 mL/min), severe hepatic impairment, or with concomitant P-glycoprotein and/or strong CYP3A4 inhibitors. Although the trials studied a dose of 0.5 mg daily, daily dosing of 0.5 mg or 0.6 mg may be considered. There are ongoing trials studying the efficacy of colchicine in patients after MI.

11.5. Immunization

Recommendation for Immunization Referenced studies that support recommendation are summarized in the Evidence Table.		
COR	LOE	Recommendation
1	A	1. In patients with ACS without a contraindication, annual influenza vaccination is recommended to reduce the risk of death and MACE.[1–4]

Synopsis

Influenza infection is associated with increased risks of cardiovascular morbidity and mortality.[5] Previous studies have shown that influenza infection may contribute to atherogenesis and plaque destabilization, thereby precipitating the occurrence of ACS.[6,7] Influenza vaccine has been shown to reduce the risk of death and MACE in patients after ACS and ASCVD and should therefore be administered in patients without contraindication.[1–3,5,8] Other illnesses such as COVID-19 and pneumococcal pneumonia increase risk of cardiovascular events and death in patients with ASCVD. However, randomized trial data are lacking to support routine administration of other vaccines for patients at time of hospitalization for ACS. As such, regular immunization schedules are supported for all patients per the US Centers for Disease Control and Prevention recommendations in the absence of contraindication.[9]

Recommendation-Specific Supportive Text

1. In the FLUVACS (Flu Vaccination in Acute Coronary Syndromes and Planned Percutaneous Coronary Interventions) study, cardiovascular death was lower in patients who received influenza vaccination compared with the control group at both 6-month (2% versus 8%) and 1-year follow-up (6% versus 17%). The triple composite endpoint of cardiovascular death, nonfatal MI, and rehospitalization for severe recurrent ischemia at 1 year was significantly lower in the vaccine group compared with controls.[2,10] Among patients admitted with MI or high-risk coronary heart disease, influenza vaccine administered within 72 hours of an invasive coronary procedure or hospitalization resulted in a lower risk of the composite primary outcome of all-cause death, MI, or stent thrombosis and a lower risk of cardiovascular death compared with placebo at 1 year.[1]

12. EVIDENCE GAPS AND FUTURE DIRECTIONS

The treatment of ACS has been the subject of thousands of clinical trials comprising very large numbers of patients. As such, its management is guided by the largest evidence base in clinical medicine. Despite this, there are numerous unanswered questions, evidence gaps, and areas for further study. Some of these areas have been addressed by observational studies but were not included in this guideline because the LOE was insufficient to guide clinical practice. Other areas were not included because they are less well defined and require more detailed study. This section summarizes some higher priority evidence gaps and areas for future study.

INITIAL EVALUATION AND MANAGEMENT

Although the 2025 ACS guideline recognizes the value of risk scores in estimating the risk of death or recurrent MI, limited prospective randomized data are available as to whether risk scores should be used to determine treatment strategies. The highest risk patients are those who present after a cardiac arrest. Although the data support an invasive approach in patients who have been resuscitated and who have evidence of ST-segment elevation on the postarrest ECG, any potential benefit of coronary angiography may be attenuated in those who are comatose. Similarly, it is less clear whether reperfusion with either fibrinolysis or primary PCI provides clinical benefit in patients with ST-segment elevation who present late after symptom onset (12 to 48 hours) but who are no longer symptomatic. Further research is needed to define the role of coronary angiography and revascularization in these patient subgroups.

In-Hospital Management of ACS

Patients with ACS are placed on telemetry to monitor for life-threatening arrhythmias or for rhythm disturbances that may require further therapy (eg, atrioventricular block, AF). Given the length of stay for most patients with ACS has decreased significantly, the optimal duration of telemetry monitoring with contemporary management is unclear. The increasingly rapid triage and timing of invasive risk stratification also calls into question the value of "preloading" of oral P2Y12 inhibitors, with preloading defined as administering the loading dose prior to coronary angiography. As outlined in this document, clinical trials of preloading have not shown a compelling benefit when coronary angiography occurs rapidly after the patient's clinical presentation. Nonetheless, the pharmacodynamic

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effects of clopidogrel are delayed due to its need to be metabolized to its active metabolite, and there are reports that the antiplatelet effects of all P2Y12 inhibitors may be delayed in patients with STEMI. In this context, parenteral P2Y12 inhibition could be considered but has not yet been compared to a strategy of more potent oral P2Y12 inhibitor administration. Other drug therapies in need of further evaluation in the ACS setting include the utility of sacubitril-valsartan, nonstatin lipid-lowering therapies (including clinical outcome studies for PCSK9 inhibitors early after ACS), and GLP-1 receptor agonists for reducing short- and long-term MACE after ACS. The clinical benefit of beta blockers in the setting of patients with NSTE-ACS requires further study, as well as the optimal duration of their use after ACS.

For patients with MVD found during coronary angiography, there are several remaining gaps in evidence. In patients with NSTEMI, the role of multivessel PCI versus culprit-only PCI needs further supportive data. As a corollary, whether multivessel PCI in the ACS setting should be guided by angiography or physiology is still a matter of debate. Finally, as noted in this guideline, the recommendations for PCI of nonculprit arteries in patients with STEMI are for patients who are not intended for CABG, which is a qualifier based on the inclusion criteria of the randomized trials. The optimal strategy for patients who have more complex anatomy is less clear.

The 2025 ACS guideline includes a new recommendation regarding the management of cardiogenic shock using the microaxial flow pump MCS device. Because the benefit of this device was offset by an increase in serious complications, more data are needed to guide the selection of patients for MCS, the timing of MCS placement and duration of support, and strategies to reduce the risks of vascular complications, bleeding, and limb ischemia.

DISCHARGE STRATEGIES AND SECONDARY PREVENTION

One of the most important areas needing further clarification is the timeline defining the transition of a patient from ACS to chronic coronary syndrome. The 2025 ACS guideline does not define this largely because no data exist to guide any recommendations. Moreover, it is likely that this transition is highly individualized and accounts for the patient's risk at initial presentation, the status of residual unrevascularized CAD, control of cardiovascular risk factors, and bleeding risk with continued antithrombotic therapy. Once a patient is deemed to have transitioned to having a "chronic coronary syndrome," the question of how to or whether to de-escalate antiplatelet therapies is unclear. These decisions may also be influenced by complications of ACS requiring additional antithrombotic therapy such as LV thrombus from a large anterior wall MI. The role of DOACs in this setting appears prudent but is not supported by a robust body of data. Other complications such as post-MI pericarditis now have several therapeutic options, but no comparative data are available to help determine which approach is optimal.

With respect to long-term secondary prevention, more research is needed to determine whether home-based CR provides the same benefit as facility-based programs and results in higher rates of adherence. Randomized trials of GLP-1 receptor agonists post MI will be important to understand the role of these agents in reducing long-term risk in patients with diabetes or those who are overweight or with obesity. Finally, data are lacking on the use of high-dose aspirin in those with post-MI pericarditis, and additional data would be useful to confirm the efficacy of colchicine post ACS.

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ARTICLE INFORMATION

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Appendix 1. Author Relationships With Industry and Other Entities–2025 ACC/AHA/ACEP/NAEMSP/SCAI Guideline for the Management of Patients With Acute Coronary Syndromes

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Sunil V. Rao, Chair	New York University Langone Health System–Professor of Medicine, Director of Interventional Cardiology	NOT RELEVANT • Medpace	None	None	NOT RELEVANT • NHLBI • PHRI	NOT RELEVANT • NHLBI*	None
Michelle L. O'Donoghue, Vice Chair	Harvard Medical School–Associate Professor, Department of Medicine; Brigham and Women's Hospital–Associate Physician, Senior Investigator, TIMI Study Group, McGillycuddy Logue Distinguished Chair in Cardiovascular Medicine	NOT RELEVANT • Verve Therapeutics RELEVANT • Amgen • Novartis	None	None	NOT RELEVANT • AstraZeneca/ MedImmune (DSMB) • Janssen Pharmaceuticals (DSMB) RELEVANT • Amgen† • AstraZeneca/ MedImmune† • Merck† • Novartis†	None	None
Marc Ruel, Vice Chair	University of Ottawa Heart Institute–Professor, Division of Cardiac Surgery and Department of Cellular and Molecular Medicine	RELEVANT • Edwards Lifesciences • Medtronic • XyloC or	None	None	RELEVANT • Artivion‡ • Artivion* • AstraZeneca* • CryoLife* • Medtronic‡ • Medtronic* • PhaseBio*	None	None
John H. Alexander	Duke University School of Medicine–Professor of Medicine, Division of Cardiology	NOT RELEVANT • Akros • Antev • Artivion • AtriCure • Curis • Ferring Pharmaceuticals • Humacyte • Janssen Pharmaceuticals • Novostia • Portola† • Teikoku Pharma • Veralox RELEVANT • Bayer • Bristol Myers Squibb • Pfizer†	None	None	NOT RELEVANT • AbbVie (DSMB) • AtriCure (DSMB) • Eli Lilly/Duke University (DMC) • FDA† • Ferring Pharmaceuticals† • GlaxoSmithKline (DSMB) • NIH‡ • Theravance (DSMB) RELEVANT • Artivion† • Bayer† • Bristol Myers Squibb† • CSL Behring†	RELEVANT • Boehringer Ingelheim	None
Usman Baber	University of Oklahoma Health Sciences Center–Associate Professor of Medicine	RELEVANT • Abbott • Amgen • AstraZeneca • Boston Scientific	None	None	None	RELEVANT • Abiomed* • Idorsia Pharma*	NOT RELEVANT • Defendant, heart failure after acute MI, 2022 • Defendant, injury after PCI, 2022
Heather Baker, Patient Representative	Dorothy Simon Elementary School–Principal; Aurora University–Adjunct Professor	None	None	None	None	NOT RELEVANT • AHA SFRN‡	None
Mauricio G. Cohen	Cleveland Clinic Florida–Director, Structural Heart Interventions; Staff Physician, Interventional Cardiology, Heart & Vascular Center	RELEVANT • Baylis/Boston Scientific • Cordis	None	RELEVANT • Accumed Radial Systems†	RELEVANT • Abbott	NOT RELEVANT • SCAI‡ • Abbott*	None
Mercedes Cruz-Ruiz, Patient Representative	HealthBridge4u–Certified State Community Health Worker, Instructor	None	None	None	None	None	None

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Appendix 1. Continued

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Leslie L. Davis	University of North Carolina, Chapel Hill–Associate Professor, PhD Division, School of Nursing	None	None	None	NOT RELEVANT • AANP	NOT RELEVANT • AANP • ACC • Elsevier • *Nursing Clinics of North America* • PCNA • Sigma Theta Tau International Honor Society • Skin, Bones, Hearts & Private Parts • *The Journal for Nurse Practitioners*	None
James A. de Lemos	University of Texas Southwestern Medical Center–Professor of Medicine, Chief of Cardiology	NOT RELEVANT • LianBio† RELEVANT • Cytokinetics† • GlaxoSmithKline†	None	None	NOT RELEVANT • Amgen (DMC) • AstraZeneca (DSMB) • Beckman Coulter (Endpoint Committee)† • Eli Lilly (DSMB)† • Janssen Pharmaceuticals (DSMB)† • Merck (DSMB) • Novo Nordisk (DSMB)† • Regeneron (DSMB) • Siemens (Endpoint Committee)† • Varian Medical Systems (DSMB) • Verve Therapeutics (DSMB) RELEVANT • Abbott† • Roche Diagnostics†	None	None
Tracy A. DeWald	Duke Heart Center–Clinical Pharmacist and Assistant Consulting Professor, Department of Medicine	NOT RELEVANT • Bodyport	None	None	NOT RELEVANT • NHLBI (PI)	NOT RELEVANT • Cytokinetics‡ • Novartis (Co–PI)*	None
Islam Y. Elgendy	University of Kentucky–Assistant Professor of Medicine	None	None	None	None	None	None
Dmitriy N. Feldman	Weill Cornell Medical College, New York Presbyterian Hospital–Professor of Medicine	None	None	None	None	RELEVANT • Medtronic*	None
Abhinav Goyal	Emory University School of Medicine–Professor of Medicine (Cardiology); Professor of Epidemiology; Emory Rollins School of Public Health–Chief Quality Officer, Emory Heart and Vascular Center, Emory Healthcare	None	None	None	None	None	None
Ijeoma Isiadinso	Emory University School of Medicine–Associate Professor of Medicine; Director of the Emory Center for Heart Disease Prevention	None	None	None	None	NOT RELEVANT • Abbott (DSMB) • AHA • Eli Lilly* • Novartis* • University of Florida*	None

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Appendix 1. Continued

Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Venu Menon	Cleveland Clinic Lerner College of Medicine–Professor of Medicine; Mehdi Razavi Endowed Educational Chair; Director of the Cardiac ICU; Director of the Cardiovascular Fellowship	None	None	None	NOT RELEVANT • Edwards Lifesciences‖	None	None
David A. Morrow	Harvard Medical School–Professor of Medicine; Brigham and Women's Hospital–Section Head, Critical Care Cardiology, Cardiovascular Division	NOT RELEVANT • Inflammatix RELEVANT • Abbott† • ARCA Biopharma • Merck† • Novartis† • Regeneron† • Roche†	None	None	NOT RELEVANT • InCarda (DSMB) • Softcell† RELEVANT • Abbott† • Abiomed† • Amgen† • Anthos Therapeutics† • ARCA Biopharma† • AstraZeneca† • Daiichi Sankyo† • Eisai† • GlaxoSmithKline† • Johnson & Johnson† • Merck† • Novartis† • Pfizer† • Regeneron† • Roche† • Siemens†	None	None
Debabrata Mukherjee	Texas Tech University–Professor and Chair, Department of Internal Medicine, Chief, Cardiovascular Medicine	NOT RELEVANT ACC†	None	None	None	NOT RELEVANT NIH‡	None
Elke Platz	Brigham and Women's Hospital–Assistant Professor of Medicine, Cardiovascular Division; Harvard Medical School–Associate Professor of Emergency Medicine	None	None	None	None	NOT RELEVANT • AHA† • Cambridge University Press • CVCT Future Clinical Trialist fellowship • *European Heart Journal-Acute Cardiovascular Care*‡ • *European Journal of Heart Failure*‡ • NIH† • Women As One‡ RELEVANT • AstraZeneca	None
Susan B. Promes	Pennsylvania State University–Professor and Chair, Department of Emergency Medicine	None	None	NOT RELEVANT • ROMTech	None	NOT RELEVANT • ACEP • McGraw Hill† • Penn State University Department of Emergency Medicine† • SAEM†	None
Tanveer Rab	Emory University School of Medicine–Professor of Medicine, Interventional Cardiology	None	None	None	None	NOT RELEVANT • ABIM • ACC‡ • Medtronic • SCAI	None
Sigrid Sandner	Medical University of Vienna–Associate Professor of Cardiac Surgery	None	None	None	None	NOT RELEVANT • *Annals of Thoracic Surgery*, Senior Editor • Marizyme, Inc.	None

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Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Yader Sandoval	Minneapolis Heart Institute, Abbott Northwestern Hospital–Interventional Cardiologist; Center for Coronary Artery Disease; Minneapolis Heart Institute Foundation–Investigator	RELEVANT • Abbott† • GE Healthcare • Philips† • Roche† • Zoll	RELEVANT • Philips† • Roche†	NOT RELEVANT • Patent‡	NOT RELEVANT • AHRQ (DSMB) • IFCC Committee on Clinical Applications of Cardiac Bio-Markers‡ • NHMRC (CEAC)‡	NOT RELEVANT • *JACC: Advances*	None
Rachel Schunder§	AHA/ACC–Science and Health Advisor, Guidelines	None	None	None	None	NOT RELEVANT • AHA/ACC salaried employee	None
Binita Shah	New York University Grossman School of Medicine–Associate Professor of Medicine; VA New York Harbor Healthcare System–Interventional Cardiologist	NOT RELEVANT • Horizons Therapeutics • Terumo Medical RELEVANT • Boston Scientific • Philips Volcano†	None	None	NOT RELEVANT • CRF (CEC) • Novo Nordisk† • The Icahn School of Medicine at Mount Sinai (CEC)	NOT RELEVANT • Abiomed * • Alleviant* • *Circulation: Cardiovascular Interventions*† • Idorsia* • PHRI* • SCAI‡ • NHLBI • VA Office of Research and Development	None
Jason P. Stopyra	Wake Forest School of Medicine–Professor, Department of Emergency Medicine	NOT RELEVANT • Cytovale RELEVANT • Roche	None	None	NOT RELEVANT • AHRQ† • Comprehensive Research Associates, LLC • Forest Devices • HRSA† • The Duke Endowment† RELEVANT • Abbott • Chiesi • Genetesis • Polymedco	None	NOT RELEVANT • Defendant, tendon injury, 2022 • Plaintiff, pulmonary embolus, 2022 • Plaintiff, glaucoma, 2023 • Defendant, spinal compression, 2023
Amy W. Talbot§	AHA/ACC–Science and Health Advisor, Guidelines	None	None	None	None	NOT RELEVANT • AHA/ACC salaried employee	None
Jacqueline E. Tamis-Holland	Cleveland Clinic–Interventional Cardiologist and Institute Director for Acute Cardiac Care	NOT RELEVANT • Gaffney Educational Trust	NOT RELEVANT • EBIX‡	None	NOT RELEVANT • PHRI • Shockwave Medical‡	NOT RELEVANT • AHA‡ • Bronx Lebanon Hospital‡ • Concepts Medical* • Encore Medical Education • NYS • SCAI‡ • Simply K Events	None
Pam R. Taub	University of California at San Diego–Professor of Medicine; Director of Step Family Foundation Cardiac Rehabilitation and Wellness Center	NOT RELEVANT • Jazz Pharmaceuticals† • Lexicon Pharmaceuticals RELEVANT • Amgen • Bayer† • Boehringer Ingelheim† • CSL Behring • Edwards Lifesciences • Eli Lilly and Company† • Esperion† • Janssen Pharmaceuticals‡ • Medtronic • Novartis† • Novo Nordisk† • Sanofi-Aventis	None	NOT RELEVANT • Epirium Bio†	NOT RELEVANT • Argenx† • AtriCure† • Dexcom • Regeneron† RELEVANT • Merck • Novartis†	NOT RELEVANT • Milestone Pharmaceuticals	None

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Committee Member	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Marlene S. Williams	Johns Hopkins Bayview Medical Center–Clinical Director of Cardiology and Associate Professor of Medicine	NOT RELEVANT • Haemonetics	None	None	None	NOT RELEVANT • Zoll	None

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*This disclosure was entered under the Clinical Trial Enroller category in the ACC's disclosure system. To appear in this category, the author acknowledges that there is no direct or institutional relationship with the trial sponsor as defined in the (ACCF or AHA/ACC) Disclosure Policy for Writing Committees.

†Significant relationship.

‡No financial benefit.

§Rachel Schunder and Amy Talbot are AHA/ACC joint staff members and acted as the Science and Health Advisors for the "2025 ACC/AHA/ACEP/NAEMSP/SCAI Guideline for the Management of Patients With Acute Coronary Syndromes." No relevant relationships to report. Nonvoting author on recommendations and not included/counted in the RWI balance for this committee.

‖The Centers for Medicare & Medicaid Services reported research funding from Edwards Lifesciences to Dr. Menon in 2023 for the ASCEND Study, Commence Pulmonary Study, and the ViV Surveillance Study, which Dr. Menon disputes.

AANP indicates American Association of Nurse Practitioners; ABIM, American Board of Internal Medicine; ACC, American College of Cardiology; ACCF, American College of Cardiology Foundation; ACEP, American College of Emergency Physicians; AHA, American Heart Association; AHRQ, Agency for Healthcare Research and Quality; CEAC, Clinical Events Adjudication Committee; CEC, Clinical Events Committee; CRF, Cardiovascular Research Foundation; CVCT, CardioVascular Clinical Trialists; DMC, Data Monitoring Committee; DSMB, data and safety monitoring board; HRSA, Health Resources and Services Administration; ICU, intensive care unit; IFCC, International Federation of Clinical Chemistry; *JACC*, *Journal of the American College of Cardiology*; MI, myocardial infarction; NHLBI, National Heart, Lung, and Blood Institute; NAEMSP, National Association of EMS Physicians; NHMRC, National Health and Medical Research Council; NIH, National Institutes of Health; NYS, New York state; PCI, percutaneous coronary intervention; PCNA, Preventive Cardiovascular Nurses Association; PHRI, Population Health Research Institute; PI, principal investigator; SAEM, Society for Academic Emergency Medicine; SCAI, Society for Cardiovascular Angiography and Interventions; SFRN, Strategically Focused Research Network; TIMI, Thrombolysis in Myocardial Infarction; and VA, Veterans Affairs.

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Appendix 2. Reviewer Relationships With Industry and Other Entities–2025 ACC/AHA/ACEP/NAEMSP/SCAI Guideline for the Management of Patients With Acute Coronary Syndromes

Reviewer	Representation	Employment	Consultant	Speakers Bureau	Ownership/ Partnership/ Principal	Personal Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Hani Jneid, Chair	Official Reviewer–ACC/AHA Joint Committee on Clinical Practice Guidelines	University of Texas Medical Branch–John Sealy Distinguished Centennial Chair in Cardiology; Professor and Chief, Division of Cardiovascular Medicine; Medical Director, Cardiovascular Service Line	None	None	None	None	None	None
Bruce M. Lo	Organizational Reviewer–ACEP	Old Dominion University–Professor/Assistant Program Director; Sentara Norfolk General Hospital–Chief, Department of Emergency Medicine	None	None	None	None	• AAEM	None
Frederick Welt	Organizational Reviewer–SCAI	University of Utah– Director, Cardiac Catheterization Laboratory	• Faraday Pharmaceuticals • Xenter, Inc.	None	None	None	None	• Defendant, perforation during angioplasty and stent placement, 2024 • Defendant, death related to spontaneous bleed, 2024 • Defendant, iatrogenic dissection of right coronary artery, 2024
Craig J. Beavers	Content Reviewer	University of Kentucky–Assistant Adjunct Professor	None	None	None	None	None	None
Theresa M. Beckie	Content Reviewer	University of South Florida–Professor	None	None	None	None	None	None
James Blankenship	Content Reviewer	University of New Mexico–Professor; University of New Mexico Health Sciences–Director of Cardiac Catheterization Laboratories	• AMA • FDA	None	None	None	• ZOLL Medical	None
Deborah Diercks	Content Reviewer	UT Southwestern Medical Center–Professor	• Celecor†	None	None	None	• Abbott Canada • Emergencies in Medicine • Quidel Corp* • Siemens • Tosoh Biomedical*	None
Clauden Louis	Content Reviewer	Winter Haven Hospital–Clinical Associate Physician	None	None	None	None	None	None
Faisal M. Merchant	Content Reviewer	Emory University–Director of Cardiac Electrophysiology	None	None	None	None	• Heart Rhythm Society	None
Noreen T. Nazir	Content Reviewer	University of Illinois at Chicago–Assistant Professor of Medicine	None	None	None	None	None	None
Derek So	Content Reviewer	University of Ottawa Heart Institute–Cardiologist	None	None	None	None	None	None
Matthew Tomey	Content Reviewer	Mount Sinai Fuster Heart Hospital–Interventional/ Critical Care Cardiologist	None	None	None	None	• McGraw-Hill Companies • AHA	None

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*Significant relationship.

†No financial benefit.

AAEM indicates American Academy of Emergency Medicine; ACC, American College of Cardiology; ACEP, American College of Emergency Physicians; AHA, American Heart Association; AMA, American Medical Association; FDA, US Food and Drug Administration; NAEMSP, National Association of EMS Physicians; SCAI, Society for Cardiovascular Angiography and Interventions; and UT, University of Texas.

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